THE MOTES-GROUP AS A MULTIPURPOSE TOOL IN ORGANIC SYNTHESIS

Dissertation

zur

Erlangung der naturwissenschaftlichen Doktorwürde (Dr. sc. nat.)

vorgelegt der

Mathematisch-naturwissenschaftlichen Fakultät

der

Universität Zürich

von

Maurizio Campagna

aus

Italien

Promotionskomitee

Prof. Dr. Jay Siegel (Vorsitz)

Prof. Dr. Stefan Bienz

Zürich, 2007

Table of contents

1. Organosilicon compounds and stereoselective synthesis

1.1. Introduction

The field of organosilicon chemistry has a rich and varied history and has long since made the progression from chemical *esoterica* to its position as a mainstay of modern synthetic chemistry. In his 1980 *Tilden* lectures, *Ian Fleming* of Cambridge University, one of the pioneers and major players in the discipline, identified the year 1968 as a watershed in the popularisation of organosilicon chemistry.[1] Not ignoring the earlier, fundamental progress of chemists such as *Eaborn* and *Jeffrey*,[2] 1968 was notable for many innovations we now take for granted, including, *e.g.*, the development of the chemistry of silyl enol ethers by *Stork* and *Hudrlik*,[3] or the introduction of the olefination reaction by *Peterson*.[4] These studies triggered a massive growth in interest to the area, which still continues in these days.

Today, nearly 40 years after the landmark publications of 1968, one could have assumed that organosilicon chemistry would have reached a state of maturity which left only a few minor areas open for new developments. A brief survey of the current literature quickly shows, however, that this is not the case. Far from atrophy, organosilicon chemistry continues to be an area of expansion, which reflects not only the sustained popularity of silicon-based reactions and reagents, but also the desire or need for new departures — such as the effective application of organosilicon compounds in transition metal-catalyzed cross-coupling reactions, the use of silanes as stoichiometric reductants in a range of chemo-, stereo-, and enantioselective catalytic reductions, or the use of chiral silicon compounds in stereoselective synthesis.

Several reasons are responsible for the current broad use of organosilicon reagents and organosilicon-based reactions:

1. Directly neighboring carbon in the same group of the periodic table, the properties of silicon are similar to (although not the same as) those of carbon.

2. The attachment and removal of silyl groups to and from organic substrates of many kinds is well established and can normally be performed under mild and selective conditions.

3. Silicon groups substantially modify both physical (boiling point, polarity, solubility) and chemical (stabilization of charges, radicals and transition states) properties of organic compounds; of these effects chemists may often take advantage in synthetic operations.

These features set the basis for silicon groups to be used broadly and efficiently in many fields of organic chemistry; from their early use as protective groups, over their application as activating groups to their use in the asymmetric synthesis, an impressive number of efficient *Si*-mediated transformations has been presented to the community in the past decades. Incidentally, the use of silicon proved quite useful not only in organic synthesis, but also in analytics — although the interest in this topic rose only recently. Particularly the use of chiral silyl moieties as chiral derivatizing agents (CDA), for a long time dimmed by *Mosher*'s discovery[5] and by a *plethora* of CDAs presented in the following decades, became in the last years more attractive with respect to the determination of enantiomeric purities and absolute configurations of labile natural products.

In the following, a short summary of some relevant examples of silicon-use in organic chemistry is given.

1.2. Organosilicon reagents and protection

Silicon has found its first role in organic chemistry as the basis of a number of protective groups. The problem of incompatibility of functional groups with certain

chemical procedures, recognized already in as early investigations as those of *Fisher* on carbohydrates,[6] is still crucial in modern organic synthesis. The construction of a molecule, even of modest complexity, can rarely be done without the use of protection. Insertion and removal of protective groups prolong a synthetic process by at least two steps, and cause an inevitable loss of yield and increase of costs. The fact that organic chemists are ready to tolerate these additional steps, however, demonstrates the intrinsic importance of protection. The synthetic potential of silicon-based protective groups was not really appreciated until the early 1970's, when a number of silyl compounds were gradually presented to the chemical community.[7-9] These reagents were used to protect alcoholic and amino functions, and their efficiency and reliability have made them soon the most versatile protective groups in organic synthesis.

The reason for the wide popularity of silicon protective groups arose from the fact that silyl ethers are readily formed as well as cleaved under rather mild conditions. In addition, their relative reactivities can be finely tuned by a simple variation of the substituents at silicon (Figure 1).

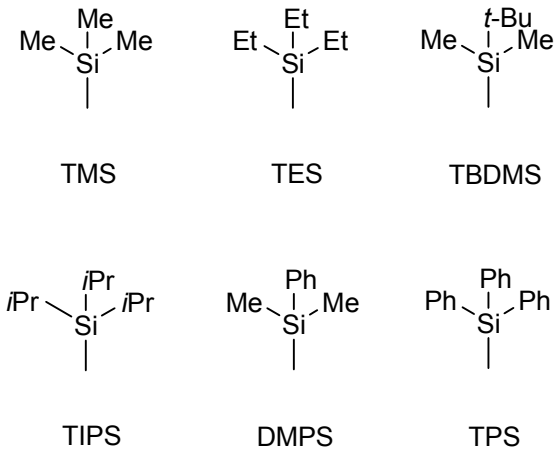
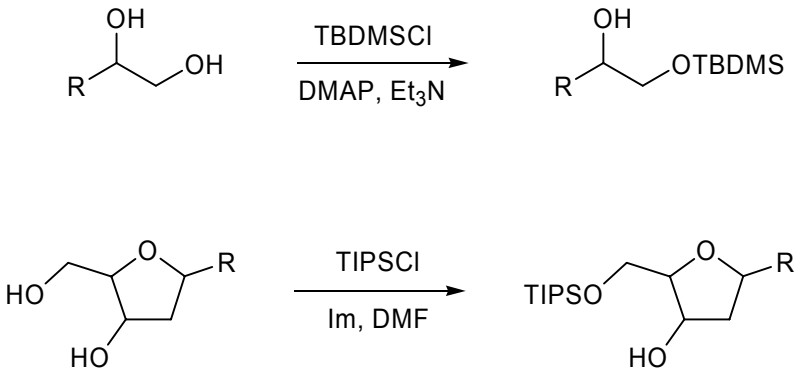


Figure 1. Common silyl ethers protecting groups

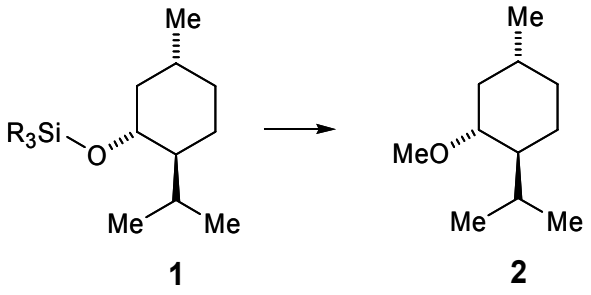
Thus, depending on the specific goal, it is nowadays possible to introduce into a molecule several silyl moieties, which behave "orthogonally" and which can be

selectively removed at the end of the process. The properties of the silyl groups are explained with steric and electronic arguments. Bulkier silyl groups are used to selectively silylate hydroxyl groups in different steric environments: an example is given in Scheme 1, where, for example, primary alcohols can be silylated in the presence of secondary alcohols. In addition, the bulkier the substituents, the lower the reactivity towards acidic and basic hydrolyses, organolithium or *Grignard* reagents, oxidation, reduction, and column chromatography.



Scheme 1

The electronic effects are responsible, *e.g.*, for the rather high reactivity of phenyl-substituted silylethers under acidic conditions as compared to purely alkyl-substituted silanes. As shown in an example in Figure 2, the rather large Ph_3Si–group can be readily removed at low pH values from compound of type **1** — almost as readily as the TMS group. Under basic conditions, however, hydrolysis is slow, as expected if steric effects were dominant.

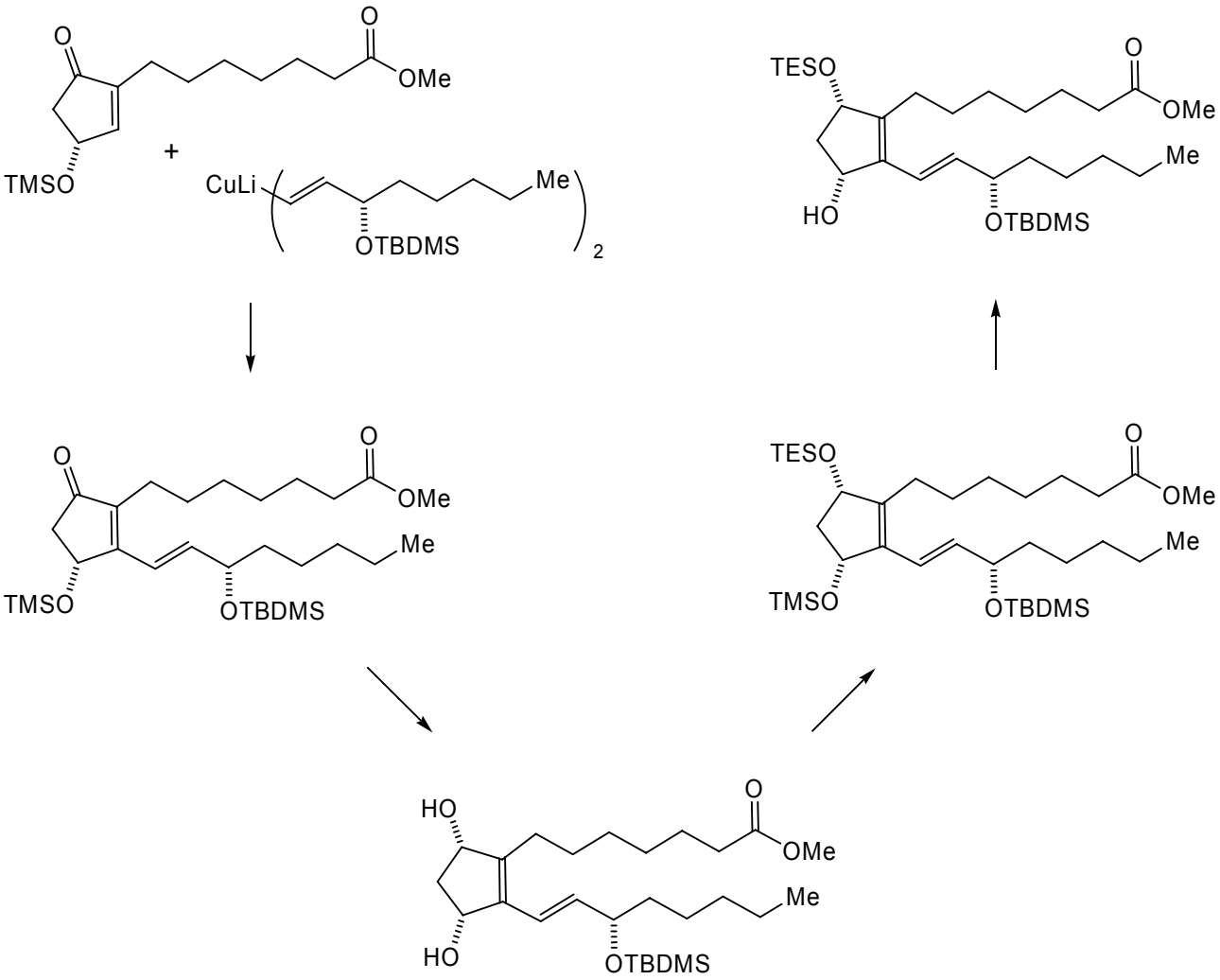


1 **2**

	R_3Si—	k_{rel}
$MeOH/MeO^-$	Me_3Si	1
	Et_3Si	0.9
	Ph_3Si	$7.7 \cdot 10^{-4}$
$MeOH/H^+$	Me_3Si	1
	Et_3Si	$2.6 \cdot 10^{-3}$
	Ph_3Si	0.16

Figure 2

Due to the combination of these effects, several transformations on complex molecules were often facilitated by the use of specific silyl moieties for the protection of functional groups, as can be seen in the synthesis of prostaglandins (Scheme 2).



Scheme 2

Moreover, silicon shows a high affinity for fluoride, and a practical consequence of the strength of the Si–F bond (142 kcal/mol *vs., e.g.,* 112 kcal mol^{-1} for Si–O or 69 kcal mol^{-1} for Si–C) is that silicon groups can be easily removed under mild and highly specific conditions using fluoride ions or HF — conditions that are compatible with many functional groups and protective groups of other types.

1.3. Organosilicon reagents and asymmetric synthesis

1.3.1. General aspects of asymmetric synthesis

It is a general opinion that most of the study on the use of silicon in protecting groups has already been done, and several reviews and books, entirely dedicated to this topic, have been published.[8-10] A lively interest, however, arose for the use of chiral silyl moieties as stereo-directing groups for stereoselective synthesis. Silicon, as the group IV element of the third row of the periodic table, is the closest relative of carbon and thus shares some important properties with the central element of organic chemistry. Like carbon, silicon favors the formation of tetrahedral structures and, like carbon, tetrasubstituted silicon moieties are chiral if the four substituents at silicon are different. In the same way as chiral carbon-based groups, chiral silanes comprise the potential to act as "vectors" for the transfer of stereochemical information from one molecular entity to another.[11] Despite the close relationship of silicon to carbon, however, the idea to use chiral silicon groups in enantioselective synthesis was not developed before the late 1970's, when the study of chirality and natural products was already in the center of the interest and several auxiliaries for asymmetric synthesis had already been presented in literature.[12]

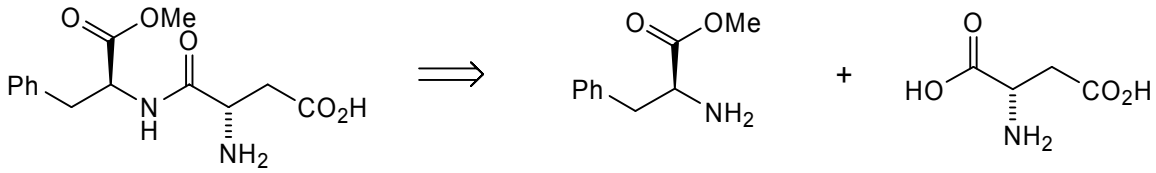
The enantiospecific synthesis of organic compounds — both natural and unnatural structures — started in fact much earlier, driven by the interest in biologically active compounds and natural products. Complex structures, such as synthetic pharmaceutical agents, display a rich diversity of molecular structures that range from very simple to astonishingly intricate. A feature common to many of these compounds is the presence of multiple stereogenic units, and control of their configurations became soon an essential element in the synthesis of many complex target molecules. Basically, this control was obtained by three different ways:

1. By assembly of enantiomerically pure chiral building blocks.

2. By modification of substrates already bearing at least one stereogenic center of defined configuration.

3. By asymmetric synthesis through external transfer of stereochemical information.

Initially, in the early 1960's, the assembly of chiral building blocks represented the easiest way to generate stereochemical complexity in a selective manner. The strategy relied on the availability of appropriate optically pure starting materials along with a *repertoire* of reactions that were suited to modify and couple the several structural moieties. As an example, the non-carbohydrate sweetener *Aspartame* (**3**), discovered in 1965[13] and possessing two stereogenic centers both of (*S*) configuration, was readily synthesized from L-aspartic acid and L-phenylalanine (Scheme 3). The idea, however, to construct complex chiral molecules from already existing chiral entities, although successful in several examples, was constrained by the rather limited pool of optically active compounds provided by nature (the "chiral pool").[14]

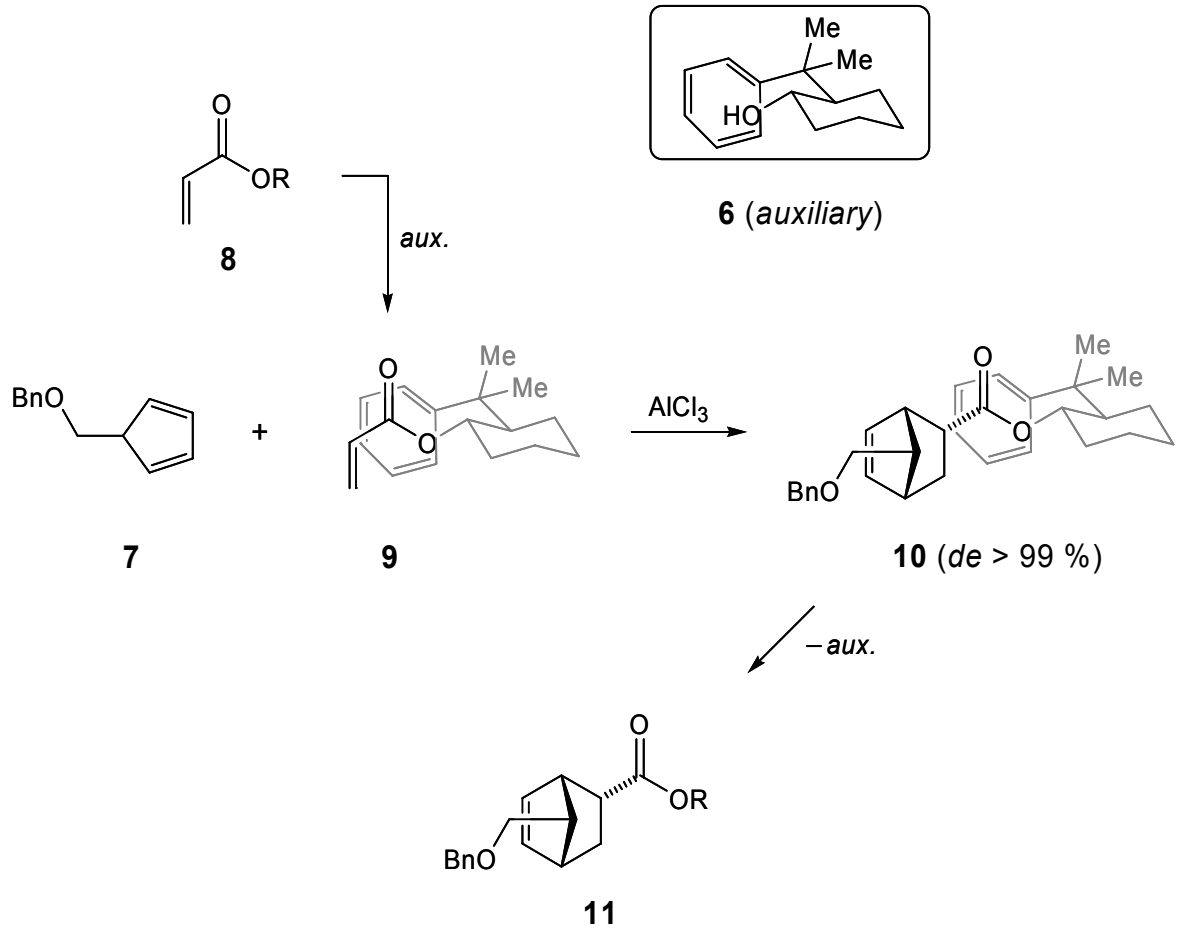


Aspartame **3** **4** **5**

Scheme 3

Still taking advantage of the "chiral pool", an alternative was presented by the development of reactions, where new stereogenic units were stereoselectively introduced into compounds under the influence of "chiral units" preexisting in the substrates. The selectivities thus obtained were inherent to the configurations of the substrates (substrate control), and a number of variations where the "chiral

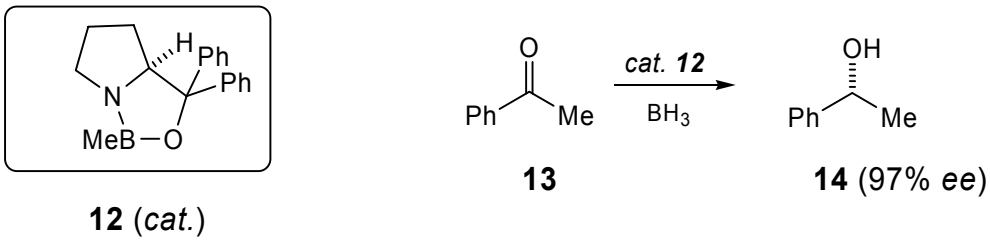
information" was brought only intermediary into the molecules through "chiral auxiliaries" were rapidly elaborated and presented.[15, 16] An example is shown in Scheme 4, where compound **11**, an intermediate in the synthesis of a prostaglandine, was prepared by means of a highly stereoselective *Diels–Alder* reaction, stereochemically controlled by a chiral auxiliary. The value of such kinds of transformations is particularly evident for cases, where several specific stereoisomers are required in the course of a synthetic project. The above mentioned approach has proven enormously powerful and certainly will play a critical role for the construction of complex molecule also in future.



Scheme 4

In the 1980's, the third strategy for the construction of chiral synthetic targets started to become popular. According to this route, new stereogenic centers were introduced

into the substrates by means of powerful chiral reagents and catalyst, which were able to induce enantioselective/diastereoselective reactions through external stereocontrol, overcoming or complementing the inherent substrate base. An example is the efficient reduction of ketone **13** with BH_3 in presence of chiral catalyst **12**, which afforded the chiral alcohol **14** with 97% ee (Scheme 5).[17, 18] With such stereocontrol the synthetic plan is no longer contingent on the properties of the substrate, but rather on the ability of reagents to exert stereoselectivity, even on complex molecule already bearing their own stereochemical information (reagent control).



Scheme 5

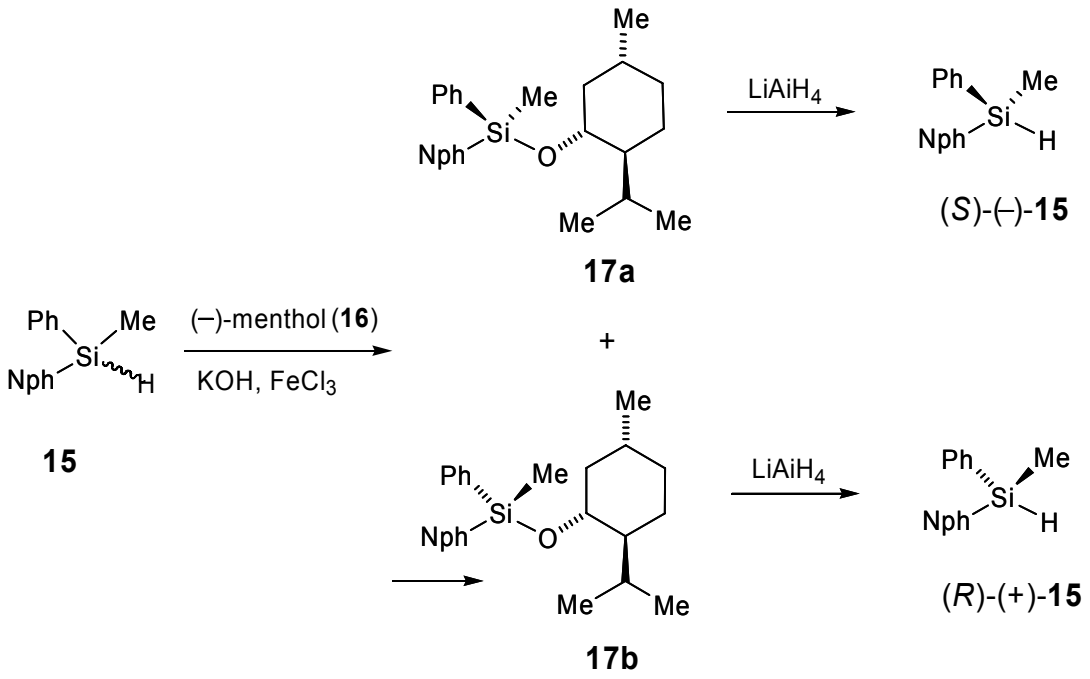
The first investigations involving the use of chiral organosilanes for the enantiospecific synthesis of organic compounds appeared in 1978; before this date, in fact, all enantiomerically enriched silanes had been prepared to study the stereochemical course of substitution reactions at the *Si*-center.[19, 20] Starting with the pioneering work of *Fry* and *Adington*,[21] studies with regard to the ability of chiral silicon groups to transfer their "chiral" information to different substrates were initiated. In the first examples, silicon groups with "*Si*-centered" chirality — denoting silicon groups where the *Si*-atom locates a center of chirality — were used as *Si*-based auxiliaries to mediate stereoselective transformations.[22, 23] For several reasons, which will be discussed below, the performance of such groups proved in most cases unsatisfactory.

However, the field of "chiral silicon auxiliaries" was expanded in the early 1980's with the preparation and the use of chiral silanes, where the stereogenic center was not directly located at the *Si*-atom but rather on one of its side chains ("*C*-centered chirality"). Such groups proved to be more efficient as stereochemical directors.

From the earliest works of *Sommer* in the 1960's[24] to the most recent examples of chiral silyl moieties, these two principal classes of silanes must be distinguished (the official definition of "*Si*-centered" and "*C*-centered" chiral silanes has to be attributed to *Paquette,*[25]) and the differences between both type of structures, as well as their use for stereoselctive synthesis, will be discussed below.

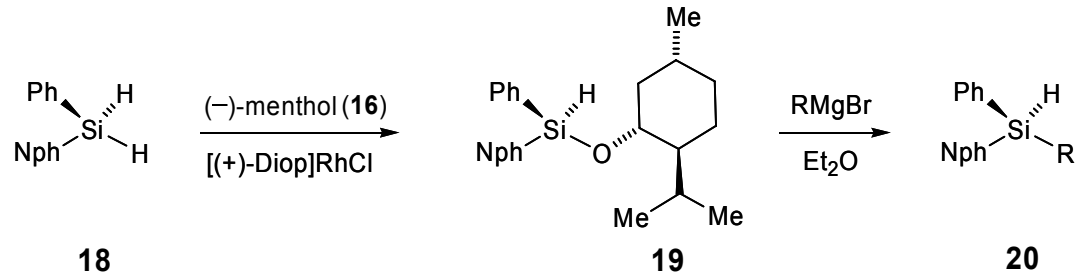
*1.3.2. "*Si-*centered" chiral silanes: preparation and reactivity*

The prototype of "*Si*-centered" silanes is methyl(naphth-1-yl)phenylsilane (**15**), which was synthesized in enantiomerically pure form by *Sommer* et *al*. already in 1959 (Scheme 6).[24] This asymmetrically substituted silicon compound was initially used almost exclusively as the starting precursor for asymmetric silicon chemistry. The preparation of (+)- and (–)-silane **15**, by resolution, represents the first example of the synthesis of enantiomerically pure silanes, possessing silicon atoms with four different substituents. Starting with tetrachlorosilane, racemic **15** was synthesized by successive substitutions. The mixture of hydrosilanes was treated with (–)-menthol **16** in presence of KOH and $FeCl_3$, and the two resulting silylethers **17a** and **17b** were separated by fractional crystallization. Reduction of each compound with $LiAlH_4$ afforded the two enantiomerically pure silanes (*S*)-(–)-**15** and (*R*)-(+)-**15**, which were subsequently converted to a variety of other chiral silanes by nucleophilic substitutions at silicon.



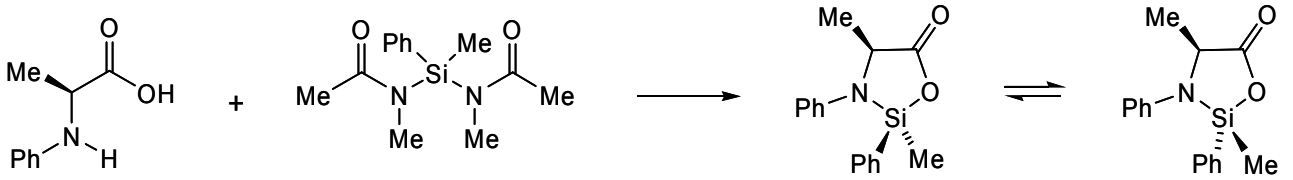
Scheme 6

At the end of the 1960's, an extension of the class of silanes with "*Si*-centered" chirality was made accessible by *Corriu* et *al*., who prepared a number of (naphth-1-yl)phenylsilanes in a stereoselective manner (Scheme 7).[26-28] The starting material was dihydrosilane **18**, which was reacted with (–)-menthol in presence of a chiral Rh-catalyst to afford silylether **19** with a de of 82%. Reaction with different *Grignard* reagents resulted in substitution of the menthol moiety, thus allowing the preparation of several enantioenriched silanes of type **20** (including (+)-**15**). The selective addition of menthol in presence of a chiral catalyst represents probably the first asymmetric functionalization of a prochiral silane.



Scheme 7

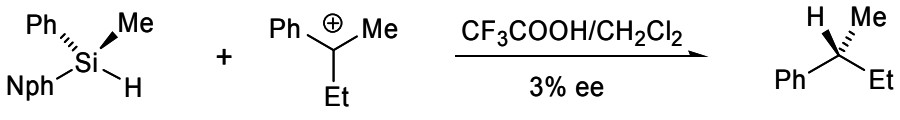
Klebe and coworkers[29] presented in 1970 the synthesis of chiral silanes with the aid of enantiomerically pure amino acids that were functionalized with a prochiral silane. As an example, the reaction of alanine derivative **21** with methyl(phenyl)-substituted silane **22** afforded the cyclic derivatives **23a** and **23b**. Since these two compounds equilibrated readily under basic conditions, crystallization in presence of KOH afforded almost quantitatively **23b** through a sort of "deracemization" (Scheme 8). Substitution reactions performed with **23b** finally gave access to a number of enantiomerically enriched chiral silanes.



21 **22** **23a** soluble **23b** precipitates

Scheme 8

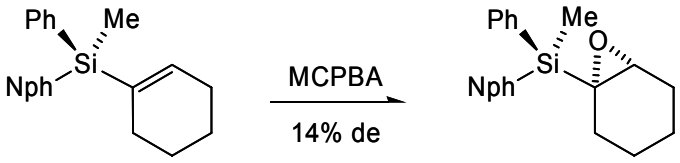
The first use of chiral silicon groups as stereodirecting auxiliaries was presented by *Fry* and *Adington* in 1978.[21] They reported on the formation of enantiomerically enriched (*R*)-2-phenylbutane (**25**) by reduction of the 2-phenyl-2-butyl cation (**24**), generated *in situ* from 2-phenylbutan-2-ol, with enantiomerically pure (*R*)-(–)-methyl(naphth-1-yl)phenylsilane (+)-(**15**) (Scheme 9). Despite the poor selectivity obtained (3% ee), the example showed that chiral silicon compounds principally can be used for enantioselective synthesis.



(+)-**15** **24** **25**

Scheme 9

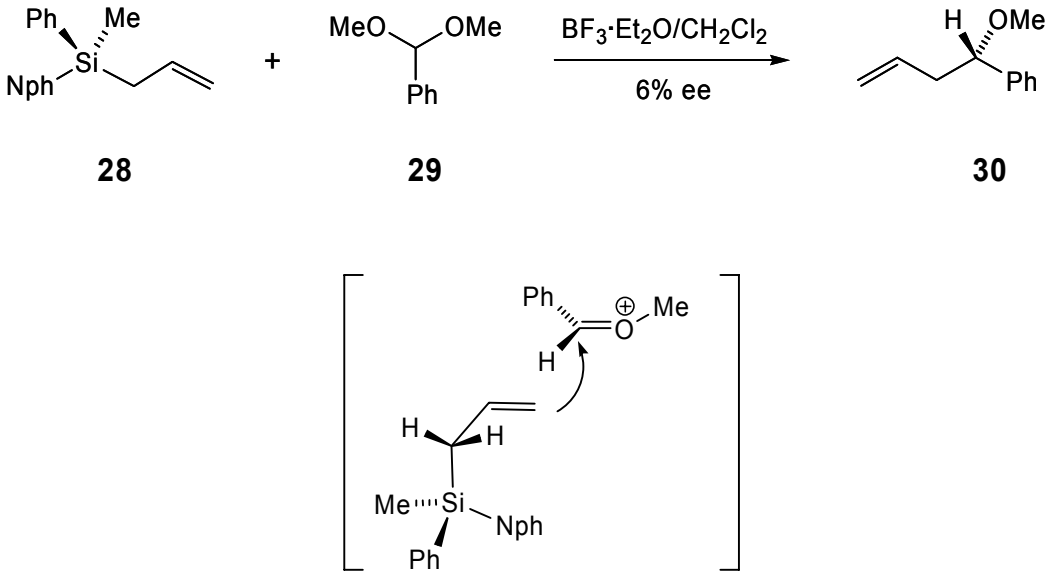
In 1982, *Daniels* and *Paquette* used the same methyl(naphth-1-yl)phenylsilyl group as a chiral auxiliary for a number of different reactions involving chirality transfer from the *Si*-center to an adjacent prostereogenic *C*-center. An example is shown in Scheme 10, where epoxidation of vinylsilane **26** with MCPBA delivered α,β-epoxysilane **27** with — still poor —14% de.[30]



26 **27**

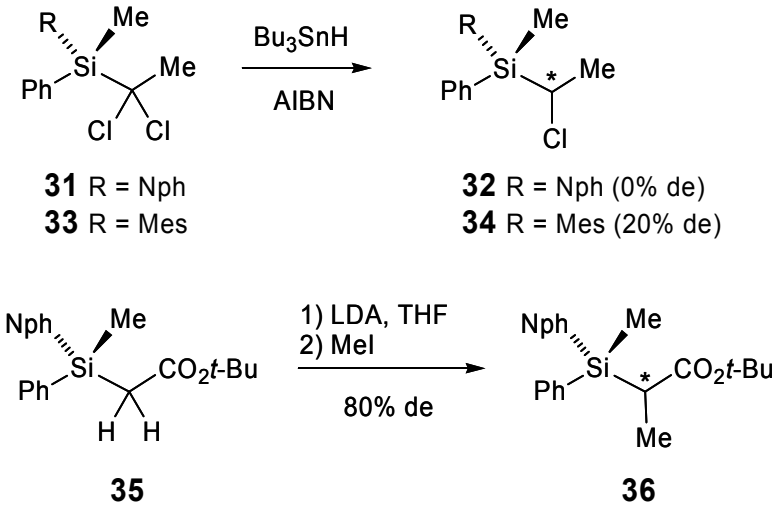
Scheme 10

One year later, *Hathaway* and *Paquette* modified *Sommer*'s methyl(naphth-1-yl)phenylsilane (**15**) by substitution of the hydrogen atom with an allyl group.[25] The idea was to test the stereoselective reductive transfer of the allyl group from the thus obtained allylic silane **28** to an oxonium ion. Low selectivities were obtained in these reactions as well. As an example, acetal **29**, when treated at –78°C in CH_2Cl_2 with silane **28** in presence of $BF_3 \cdot Et_2O$ as a *Lewis* acid, delivered homoallylic ether **30** in 67% yield and with 6% ee (Scheme 11). The low stereoselectivities obtained are probably due not only to the four-bond distance between silicon, bearing the "chiral" information, and the prochiral reaction site, but also to the spacial arrangement neccessary for the allylation reaction, placing the silicon and the electrophilic groups to the opposite faces of the π-system.



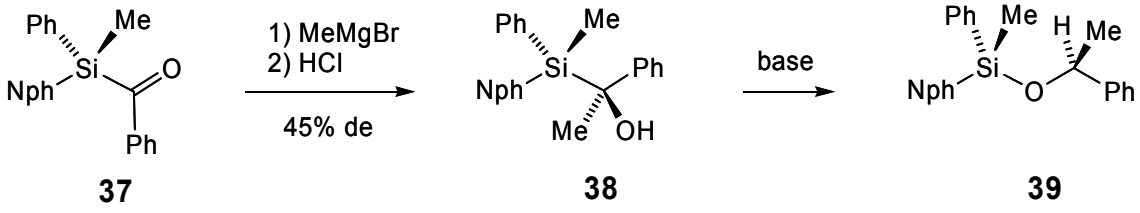
Scheme 11

In 1985, the diastereoselctive radical reduction of compounds **31** and **33** was studied by *Larson* and coworkers.[31, 32] Treatment of the two (1,1-dichloroethyl)silanes with Bu_3SnH in presence of a radical initiator afforded a racemic product **32** for the naphthyl derivative **31**, while, on the other hand, compound **33** with the sterically more demanding mesityl group delivered the respective reduction product **34** with 20% de (Scheme 12). Much higher diastereoselectivities were even obtained for the α-methylation of ester **35**, performed with LDA and MeI, which delivered **36** in 81% yield and 80% de. The relative configurations in the products were not established in both cases.



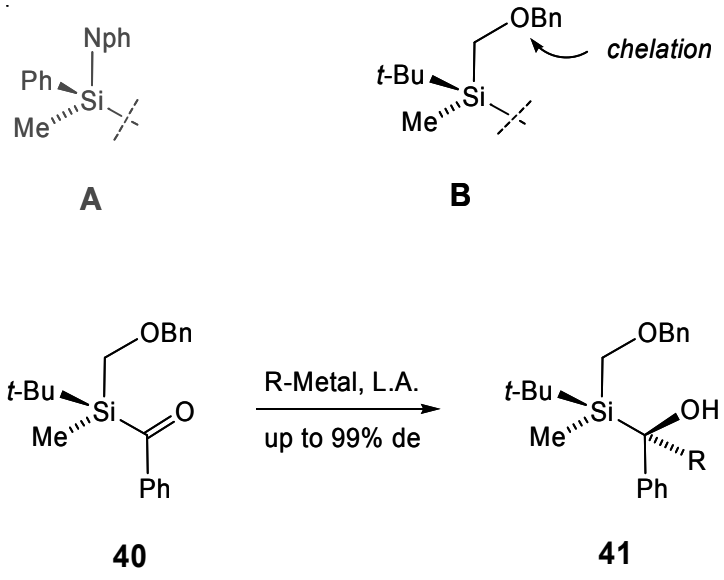
Scheme 12

In 1991, *Bonini* et *al.* studied the nucleophilc additions of organometallics to acylsilane **37** (Scheme 13) and demonstrated that the observed selectivities depended strongly on the steric effects generated by the substituents at silicon.[33] Addition of MeMgBr to acylsilane **37** — derived from *Sommer*'s hydrosilane by a three-step procedure — delivered silylcarbinol **38** with a de of 45%. This compound became the basis of a stereochemical study concerning the *Brook* rearrangement. When **38** was treated with a catalytic amount of base, alkoxysilane **39** was formed with retention of configuration at the *C*-center and at the *Si*-center. The *Brook* rearrangement is an example which clearly shows that a silyl group can be removed stereospecifically from an organic structure, even if it is directly bound to the stereogenic center.[34] This feature proved to be very important for chiral silicon groups to be used more general for stereoselective synthesis.



Scheme 13

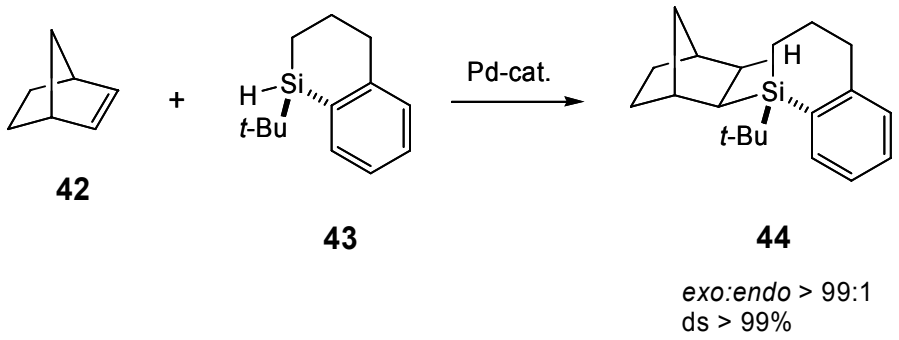
In 1997, a new concept for "*Si*-centered" chiral silicon auxiliaries was developed in Zurich (Scheme 14). Since the low selectivities attained with the "classical" auxiliaries of type **A** — possessing three rather simple and not highly variable hydrocarbon groups — was attributed to the insufficient stereo-differentiation in the transition structures effected solely by the relative sizes of the three silicon substituents, an (alkoxy)methyl group was attached to silicon (auxiliaries of type **B**). With such a group, template effects accompanied with higher selectivities were expected to become operative in reactions where intermediary chelates can be formed, such as in the 1,2-addition of organometallic reagents to acylsilane **40**. In fact, selectivities as high as 99:1 were observed for the chelate-controlled addition of *Grignard* reagents to acyl silane **40** and related compounds. Similarly, high selectivities were also found for a number of further chelate-controlled reactions with the same auxiliary such as in the 1,4-additions of organocuprates to α-silylated α,β-unsaturated ketones (up to 99% de).[35]



Scheme 14

In 2006, a transition-metal-catalyzed hydrosilylation of prochiral alkenes with "*Si*-centered" silanes was presented by *Oestreich* (Scheme 15),[36] who chose a silane

with the *Si*-center embedded into a cyclic carbon framework in order to create rigidity. The reaction, catalyzed by Pd(0), seems to proceed by a modified *Chalk-Harrod* mechanism,[37, 38] and diastereoselectivities of higher than 99% were found.



42 **43** **44**

exo:endo > 99:1
ds > 99%

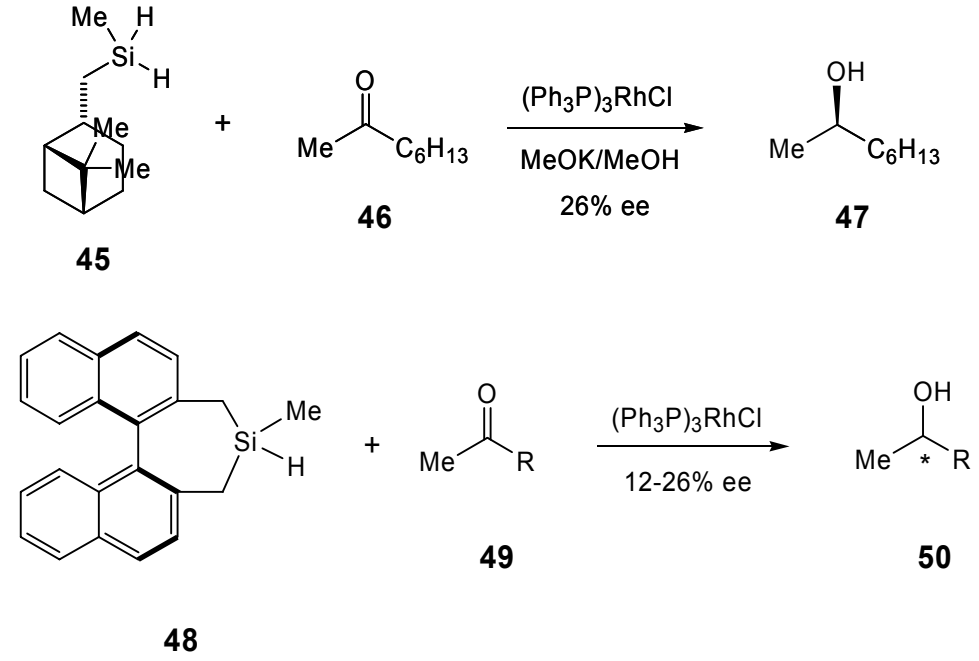
Scheme 15

As shown in this brief *excursus*, the use of stereogenic silicon as a stereochemical controller in reagent- as well as substrate-controlled transformations seems to allow excellent selectivities — but only in special cases. A reason which contributes only partially to the explanation of these results, can be found in a fundamental flaw that inherently afflicts these structures: a carbon–silicon single bond (187 pm) is substantially longer than a carbon–carbon single bond (153 pm).[39] If compared with a related "*C*-centered" chiral auxiliary, the chiral information resides with *Si*-auxiliaries further apart from the reaction site, and good selectivities can be only observed by rigidifying the structure in the transition state (*e.g.* by chelation).

But this is not the only drawback for the use of "*Si*-centered" chiral silicon groups in stereoselective synthesis: the preparation of these compounds in enantiomerically pure form is often demanding, and high risks of racemization accompany all operations of synthesis, use and recovery of the silyl moiety.

1.3.3. "C-centered" chiral silanes: preparation and reactivity

As in the case of the first "*Si*-centered" chiral silanes, the results achieved in the early 1980's by *Wang* and *Chan* with one of the first examples of "*C*-centered" chiral silanes were not very successful.[40] Reduction of ketone **46** with silane **45** as hydride donor in presence of the *Wilkinson* catalyst delivered a mixture of diastereomeric silyl ethers, which were hydrolyzed to alcohol **47**, finally obtained with 26% ee. Some years later, similar low selectivities were obatined by *Jung* and *Hogan* with their reductions of prochiral ketones with the chiral C_2-symmetric binaphthyl silane **48** in presence of a metal catalyst.[41] The desired alcohols were obtained with insufficient 12–26% ee (Scheme 16).

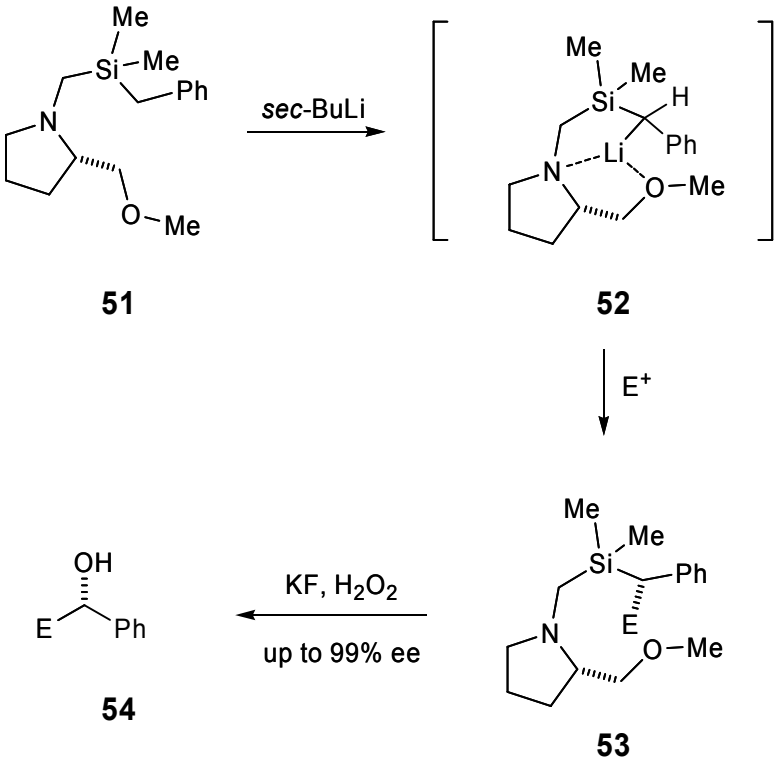


Scheme 16

Better results were obtained when the "chelate-principle" was applied to the "*C*-centered"-chiral silanes, too. Since the reason for the low selectivities could tentatively attributed to the rather long distance between the asymmetric unit of the silicon moiety and the prochiral reaction site, the introduction of chelating units —

able to bring the asymmetric units and the prochiral reaction sites into closer proximity — was tested.

Between 1989 and 1992, *Chan* and *Pellon* demonstrated that chiral α-silyl carbanions could be successfully used in asymmetric synthesis if the anion is generated in the neighborhood of coordinating sites present in the chiral auxiliary.[42] The benzylic metallation of benzylsilane **51**, *e.g.*, generated a chelated organolithium species **52**, which reacted readily with electrophiles E^+ (alkyl halides or epoxides) to afford products of type **53** with high stereoselectivities. The stereospecific removal of the silicon auxiliary through *Tamao–Kumada–Fleming* oxidation[43] delivered alcohol **54** with ee's of > 99% (Scheme 17).

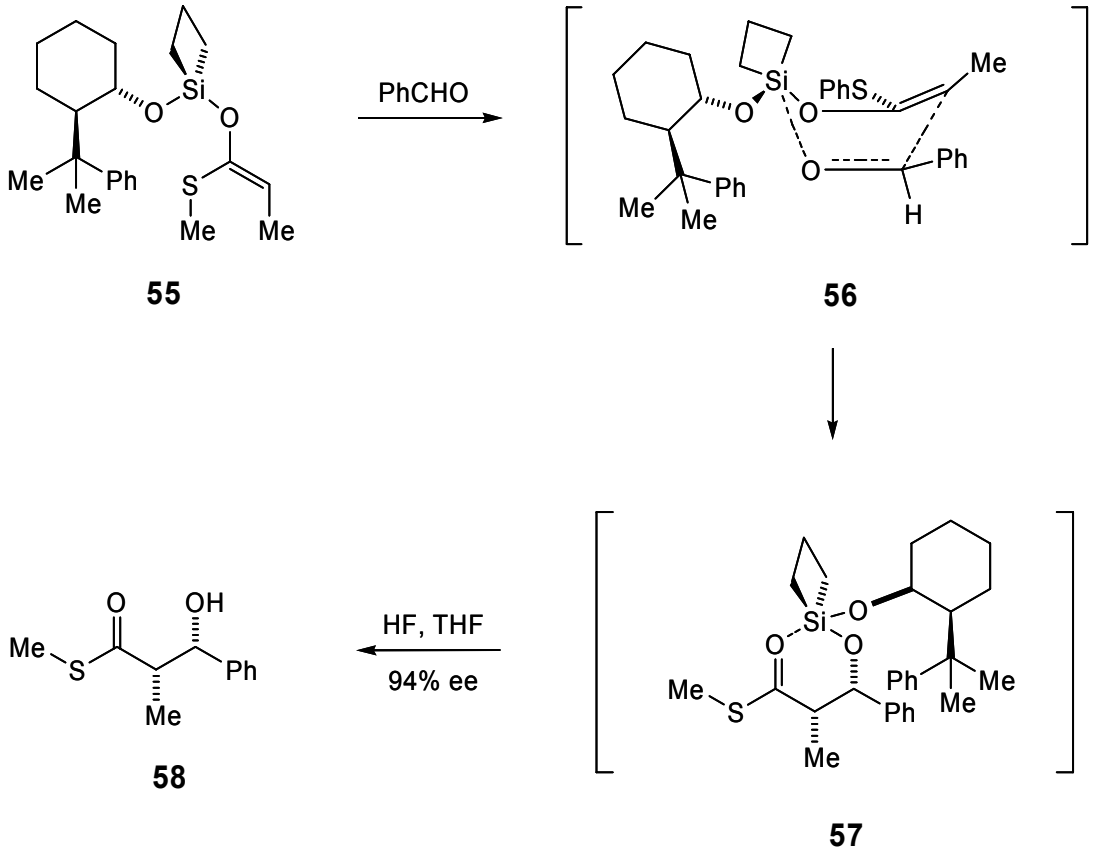


51 **52** **54** **53**

Scheme 17

In 1994, chiral "*C*-centered" silanes were employed by *Denmark* in *syn*-selective asymmetric aldol reaction.[44] For example, asymmetric allyl-modified *S*,*O*-(alkoxysilacyclobutyl)ketene acetal **55** deliverd aldol **58** with high diastereo- and

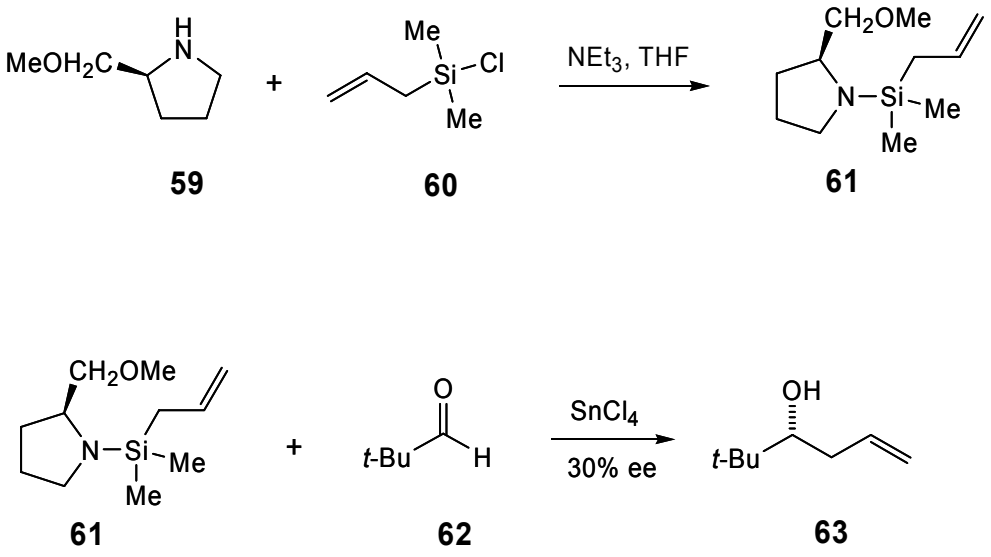
enantioselectivity (94% ee). The *syn* selectivity of the process was explained by a direct intramolecular silicon transfer *via* a boat-like transition state, with silicon acting in the strained four-membered ring as an intramolecular *Lewis* acid (Scheme 18).



Scheme 18

The high selectivities found by *Chan*, *Pellon,* and *Denmark* with their stereoselective transformations show that the "chelate-principle" is in fact applicable to "*C*-centered" chiral silicon groups as well. Coordination of reagent and substrate through an external *Lewis* acid or silicon itself rigidifies the transition structures, brings the the stereogenic unit of the auxiliary in closer proximity to the reaction site, and thus effects high selectivities.

That this is not always necessarily the case, however, is shown with the following example, where a new class of silafunctional reagents, based for the first time on aminosilanes, was prepared and tested by *Bonini* et a*l* (Scheme 19).[45] With the attachment of the aminoether substituent to the allylic silane, the authors attempted to bring the silicon and the carbonyl groups to the same face of the π-system of the allylic moiety, expecting more interaction of the chiral moiety of the auxiliary with the prochiral unit of the substrate. Indeed, allylsilane **61**, deriving from **60** by modification with a proline-derived framework, reacted with pivaldehyde in the presence of a stoichiometric amount of $SnCl_4$ to the expected homoallylic alcohol, however, with solely 30% ee (Scheme 19). The reason for this low selectivity is not known; most likely the allylation occurs, despite the donating group attached to silicon, still in an *anti*-fashion — the metal not being jointly complexed to the auxiliary and to the substrate.



Scheme 19

In conclusion, "*C*-centered" chiral silicon auxiliaries, when used in chelate-controlled transformations, proved as efficient as "*Si*-centered" chiral silicon groups for stereoselective transformations. They appear, however, to be more versatile than their counterparts since the unit of asymmetry is located on the carbon framework.

Particularly the risk of epimerization/racemazation at a stereogenic *Si*-center is not existent with such compounds, allowing their more general use under mild as well as harder reaction conditions. Additionally, optically active silanes might be obtained from precursors of the chiral pool.

1.4. Organosilicon-based chiral derivatizing agents.

Chiral silicon compounds have recently found application as chiral derivatizing agents for analytics. As discussed in the previous section, the need to obtain enantiomerically pure products has produced an immense growth in the field of asymmetric synthesis, in which the availability of simple and reliable methods for the determination of enantiomeric purity and absolute configuration is a must. The interest on this topic, in fact, stems from the widely recognized fact that the stereochemistry of compounds often determines their important properties with respect to chemical, physical, biological, and pharmaceutical aspects. Basic methods for the determination of enantiomeric purities comprise, among others, integration of high-performance liquid chromatograms or gas-liquid chromatograms (HPLC/GLC on chiral stationary phases or with diastereomeric derivatives), while the assignment of absolute configurations relies principally on single crystal X-ray crystallography, even though chiro-optical methods (*e.g.*, circular dichroism (CD), optical rotatory dispersion (ORD), or specific optical rotation) are possible for specific compounds as well. However, their use is not devoid of some inconveniences and limitations related to the equipment, which is very specific to the method and requires special training for operation, as well as to the sample which, in the case of X-ray diffraction (XRD), requires monocrystals of good quality and compound possessing heavy atoms.

The most direct approaches to the problem of determining enantiomeric purities and absolute configurations have emerged from NMR spectroscopy.[46] These techniques are particularly appealing, because of unquestionable advantages, which include the

following: (a) the instrumentation is available in most laboratories; (b) an in-depth understanding of the fundamentals of the method is not necessary to apply it; (c) only a small amount of sample is needed, and this can be recovered; and (d) the analysis is performed with dissolved samples and thus applicable to both solid and liquid compounds.

Two general approaches are known:

1. In the first approach, derivatization of the substrateof interest is not necessary: the sample (*e.g.*, a pure enantiomer or a mixture of enantiomers) is analyzed directly by NMR in a chiral environment that is provided by a chiral solvent or by the addition of a chiral solvating or shift agent (CSA).[47] In this approach, no covalent linkage between the substrate and the chiral "reagent" exists. This is certainly an advantage but also the origin of limitations. The chiral environment, in fact, might produce too small differences in chemical shifts for the two enantiomers whose NMR are very similar; often, both enantiomers must be available for comparison, and no clear-cut correlations between the absolute configuration and the NMR spectra can be established. For those reasons, the value of this method is practically restricted to the determination of enantiomeric purities.[48-50]

2. The second approach involves derivatization of the substrate (*e.g.*, a pure enantiomer or a mixture) with one or both of the two enantiomers of a chiral derivatizing agent (CDA),[51, 52] producing two diastereomeric derivatives. In this case, the chiral environment is provided by the auxiliary reagent; the association with the substrate is covalent and leads usually to more substantial differences in chemical shifts for the individual enantiomers than those obtained with CSAs. Additionally, due to the defined connectivities in the diastereomeric derivatives, rules for direct determination of absolute configurations for certain types of compounds could be discerned, the most

famous being the *Mosher* method to deduce the absolute configuration of secondary alcohols.[5] Although in certain cases a combination of the two approaches has been used (*e.g.*, the addition of lanthanide shift reagents to the CDA derivatives),[52] the derivatization with chiral auxiliary reagents is, by far, the method of choice for the assignment of absolute configuration by NMR.

Typically, the changes of chemical shifts for nuclei neighboring the asymmetric carbon of a substrate (L_1 and L_2) are particularly prominent in the diasteromeric derivatives and are thus followed in most of the cases. These differences in chemical shifts, expressed with values of Δδ, can provide information about the absolute configuration of a center of chirality if the algebraic signs (+ or –) of the Δδ-values are consistent throughout a series of homochiral compunds (Figure 3).

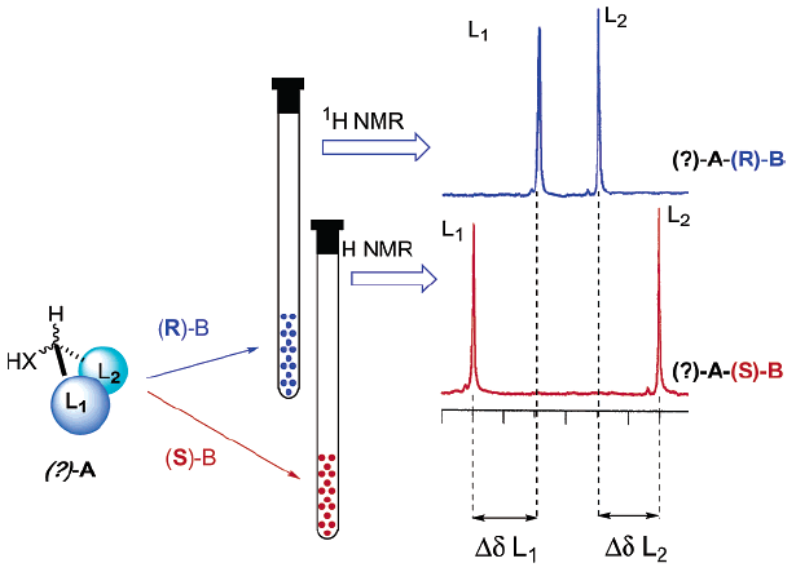


Figure 3 (from J. M. Seco, E. Quiñoá, R. J. Riguera, *Chem. Rev.* **2004**, *104*, 17).

Many efforts to develop CDAs that are useful to assign the absolute configuration of different substrates have been described.[53-55] Since its implementation in 1973, the so-known "*Mosher* method", however, which uses MTPA[(methoxy)(trifluoromethyl)(phenyl) acetic acid)] as the reagent in its original description, has

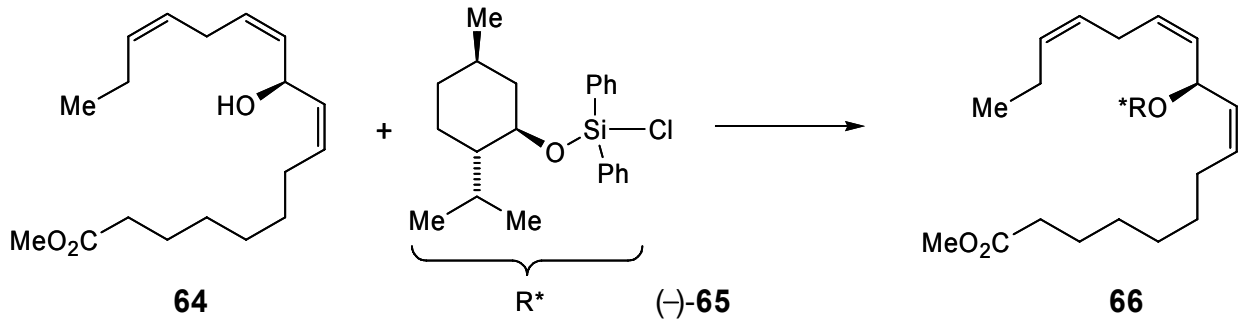
been the most successful, giving way in its evolution to many new and more efficient reagents that are useful for different substrates and are based on the same principle. In general, the structure of the chiral auxiliary reagent must incorporate groups with specific functions:

1. A polar or bulky group, to fix a particular conformation.

2. A functional group (*e.g.*, carboxylic acid), that provides a site for covalent attachment of the substrate.

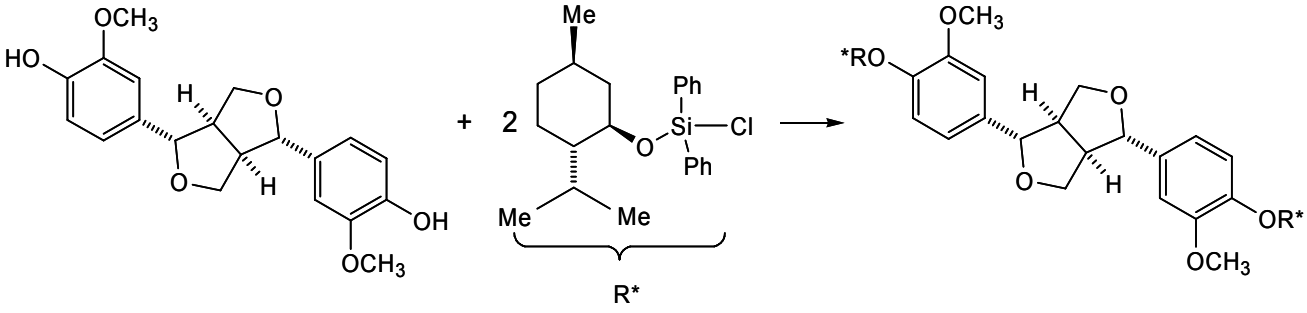
3. A group, that is able to produce an efficient and space-oriented anisotropic effect (*e.g.*, aromatic or carbonyl groups) to selectively effect different shielding or deshielding for the substituents L_1 and L_2 of the substrate.

Although a silicon moiety seems to fit the above explained description of an ideal CDA, the field of *Si*-based CDAs is not rich of examples. One of the few attempts to use chiral silylating reagents to determine the enantiomeric purities of chiral allylic alcohols was presented by *Meinwald* and coworkers in 2000.[56] The heat- and acid-sensitive alcohol **64** proved incompatible with MTPA-derivatizations, due to facile elimination of the esterified hydroxyl group (leading to a mixture of conjugated tetraenes). A "*C*-centered" chiral chlorosilane **65** was developed, and the diastereomeric silyl ethers resulting from its reaction with alcohol **64** were readily distinguished by ^{1}H-NMR (Scheme 20).



Scheme 20

The same authors proposed some years later a procedure for the assignment of the absolute configuration of the insect defensive agent pinoresinol (**67**).[57] Initially, diol (+)-**67** (of known configuration) was derivatized with (+)- and with (–)-chloromenthoxydiphenylsilanes (**65**) and the ^{1}H-NMR-spectra of these derivatives were recorded; comparison of these spectra with the one obtained from the unknown sample derivatized with (–)-**65**, revealed the configuration of the extracted compound (Scheme 21). This procedure was tested with good results on other natural products too.



(+)-Pinoresinol (**67**) (–)-**65** **68**

Scheme 21

1.5. The MOTES group: design and preliminar experiments

A closer look throughout the chemistry of silicon, here briefly presented and reviewed, shows that silicon compounds are nowadays worldwide used as versatile protective groups, and that chiral silicon moieties, in particular, prove to be extremely useful as auxiliaries for stereoselective transformations. Recently,*Trzoss* et *al.* have designed a new chiral silicon reagent: (*R*)-(1-methoxy-2,2,2-triphenylethyl)dimethylsilane **69b**, shown in Figure 4 together with the X-ray structure of the phenyl derivative, **70**.[58]

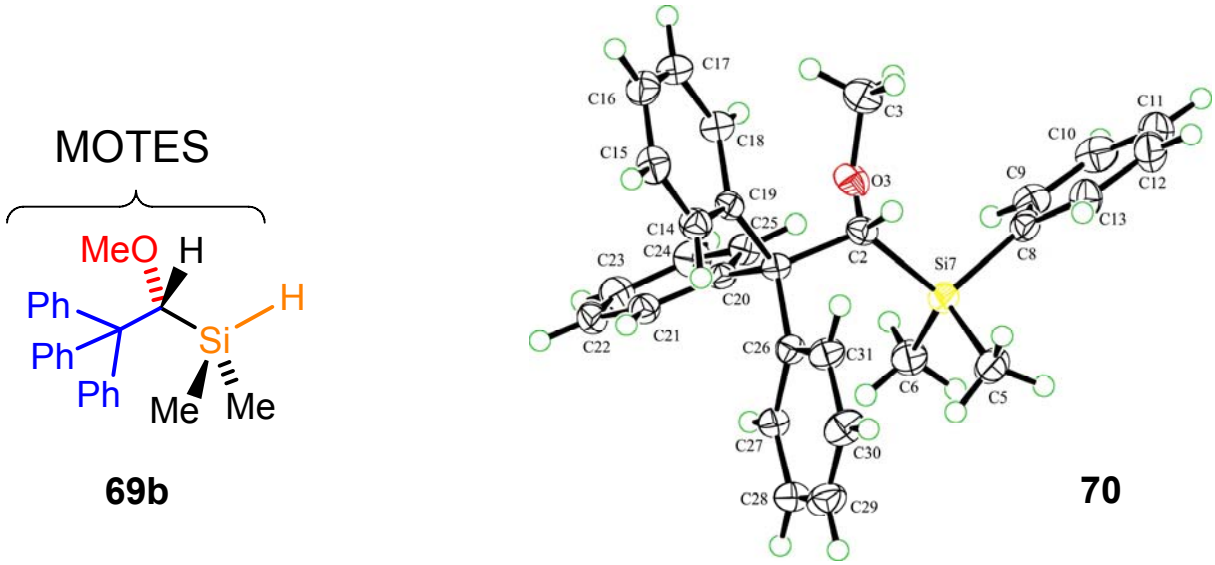


Figure 4. Structure of the MOTES-H (**69b**) and X-ray structure of MOTES-Ph (**70**)

MOTES-H is a chiral molecule and possesses a stereogenic center on the side chain of one of the substituents attached to silicon. The three phenyl groups ensure a considerable steric hindrance and block the rotation around the Si-C bond, so that a nucleophile can hardly attack silicon; thus, MOTES-derivatized substrates are stable under basic as well as slightly acidic conditions, and can be safely chromatographed on silica gel (Figure 5).

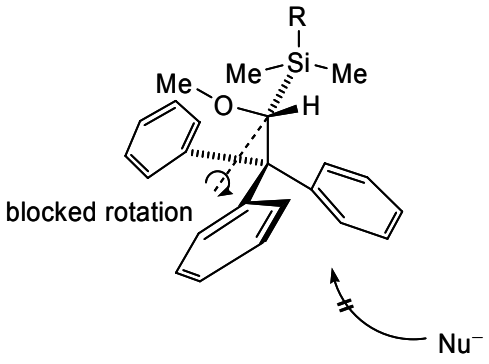
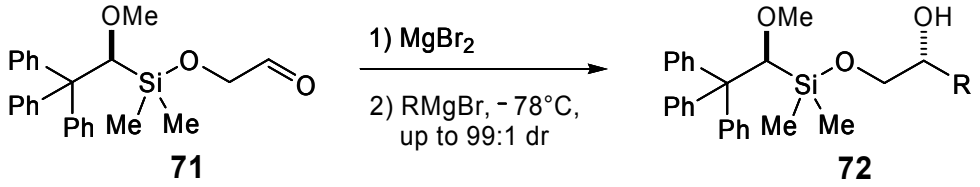


Figure 5

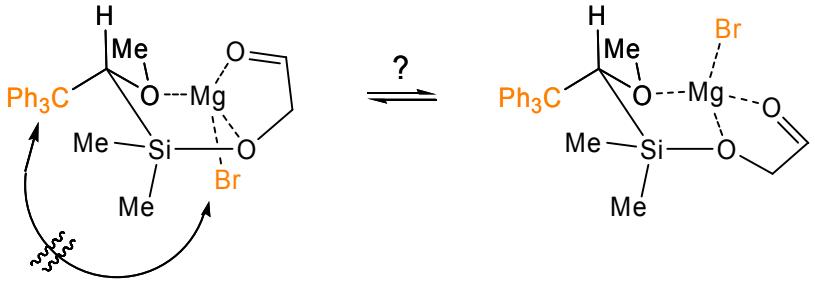
The function of the MeO group in **69b** is to act as a *Lewis* base towards a *Lewis* acid, added to the reaction mixture to be chelated. As pointed out before, asymmetric

induction on specific reactions can be obtained when a rigid structure is formed in the transition state, and we have recognized that chelation can contribute dramatically in this sense, creating rigid cyclic intermediates which aid stereochemical control. In order to prove whether these effects are operative for reactions with MOTES-derivatized substrates, a set of additions to (*rac*)-α-silyloxyaldehyde **71** was performed by *Trzoss* and, in fact, dr up to 99:1 were obtained in these transformations (Scheme 22).[58]



Scheme 22

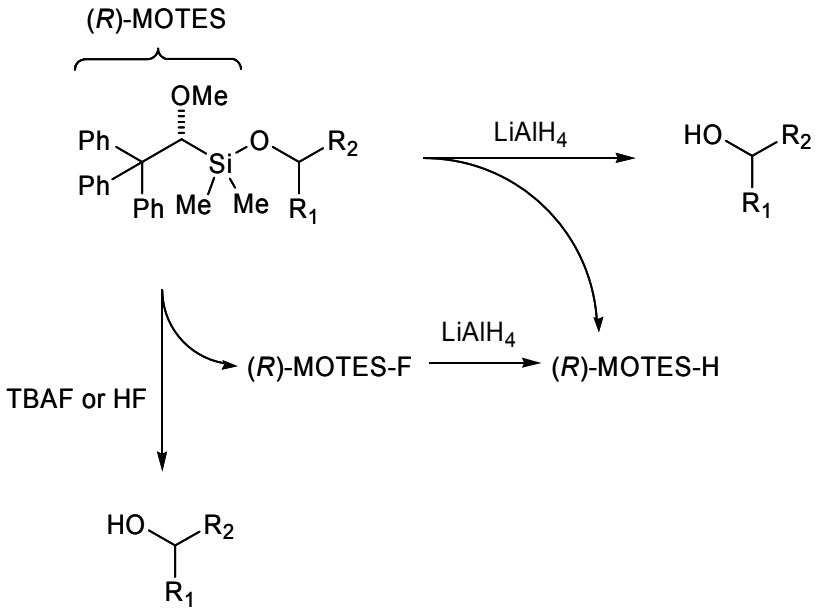
These results were confirmed by some basic theoretical calculations, which showed that, of the two possible chelate structures **C** and **D** of chelated transition states, **D** is particularly favoritable due to the weaker interactions between the trityl group and the bromine atom linked to Mg (Figure 6). Exchanging the Ph_3C group with a Me, these interactions are less pronounced and structures **C** and **D** are energetically more comparable.



	C		**D**
R = CPh_3	1	:	270000
R = Me	1	:	4000

Figure 6

The initial investigations of *Trzoss* have also shown that the MOTES group can be easily removed and almost quantitatively recovered at the end of a reaction scheme, simply by a reduction of the selected silyl ethers with $LiAlH_4$. This deprotection is quick and affords the free alcohols and MOTES-H (**69b**) as two usually well separable compounds by chromatography. When a carbonyl group (or any other functional group amenable to reduction by $LiAlH_4$) is present in the molecule, traditional deprotection with TBAF or HF can easily be employed, and the resulting Si-F bond can be reduced separately to get the auxiliary back in form of MOTES-H (Scheme 23).[58]



Scheme 23

2. Goals of the work

As shown above, the MOTES group proved to act as an efficient auxiliary for nucleophilic additions to α-hydroxyaldehydes. Encouraged by these first results, we aimed to verify whether the same stereocontrol can be obtained when **69b** is used for a broader range of substrates and reactions. The key-requirement is the intermediary formation of chelated complex which should arises by coordination of a *Lewis* acid (Mg^{2+} in our case)[59] to the *O*-atoms of the derivatized substrates. When such intermediary structures are formed, we expect to achieve considerable sterochemical control in the reaction, independently from the type of transformation; in principle, 1,2- and 1,4-additions to carbonyls, aldol reactions, cycloadditions, reductions, could all be performed in a highly selective manner with MOTES-derivatized substrates, if our hypothesis proved valid (Figure 7).

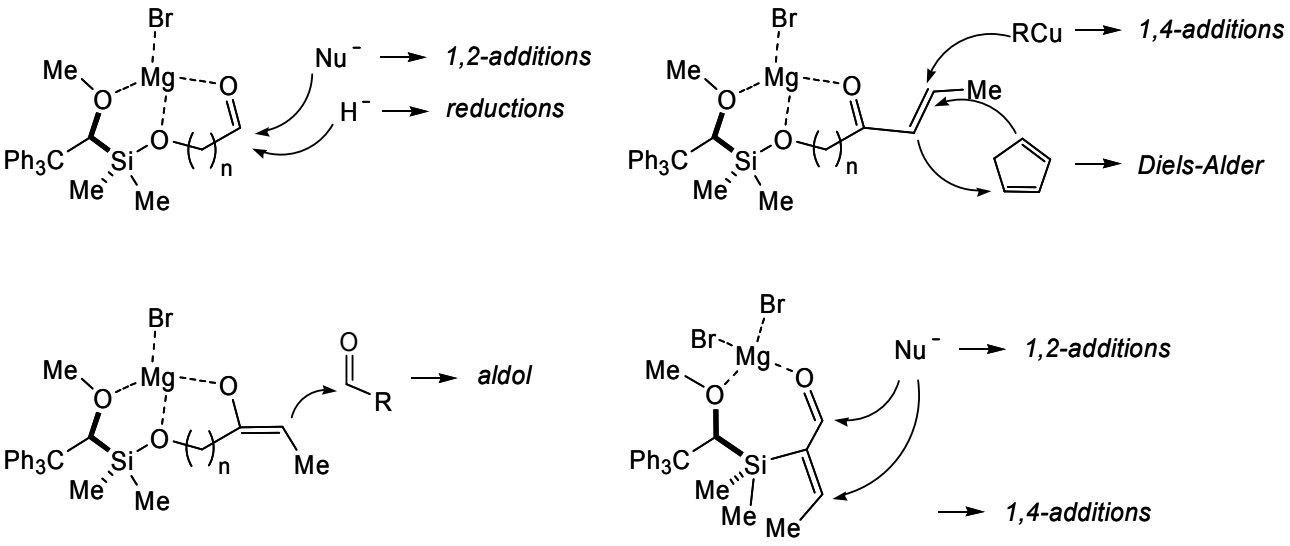


Figure 7

The ease by which we were able to distinguish the diastereomeric products of our reactions by NMR-spectroscopy, moreover, showed that the potential applications of the MOTES group are not limited to the above mentioned effects in terms of

protection and stereochemical control, but suggests that this group can also work actively (and simoultaneously) as a CDA for the quantification of enantiomeric mixtures. The three phenyl groups of the trityl moiety should be able to create a spacially distinguished anisotropy which is expected to lead to a substantial differentiation of otherwise undistinguishable protons in NMR (Figure 8). We thus would like to test MOTES-H as a chiral derivatizing agent (CDA) to enable quantification of mixtures of enantiomeric products, as well as — if possible — determination of absolute configurations.

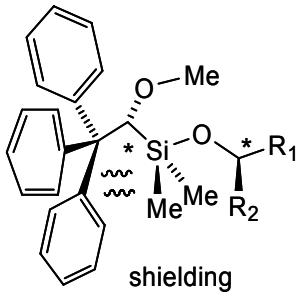


Figure 8

3. Own investigations

The present work can be schematically divided into three parts:

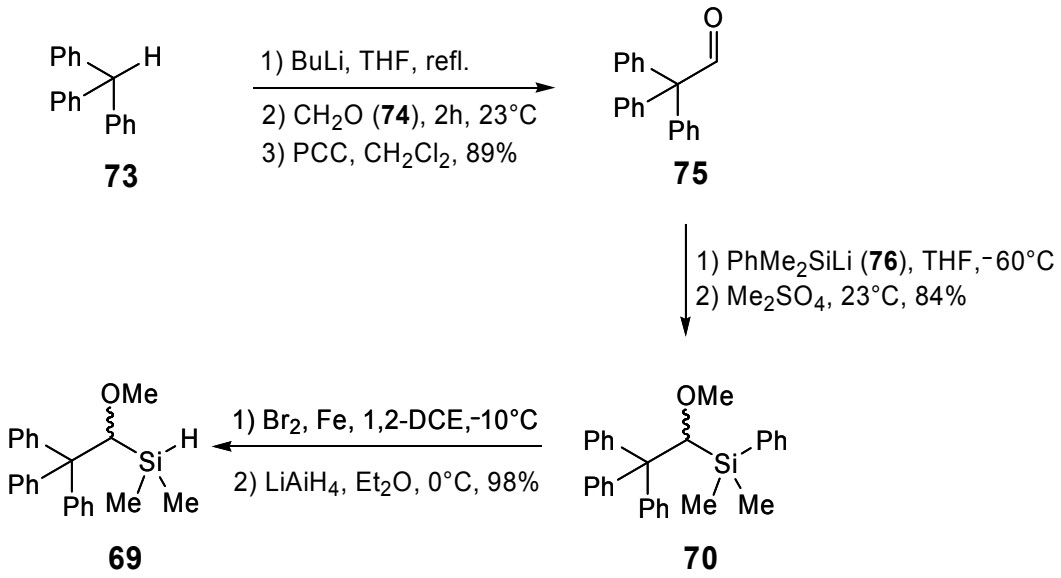
- The synthesis of the MOTES group.
- Investigations of substrates where **69b** is connected through a Si–O bond.
- Investigations of substrates where **69b** is connected through a Si–C bond.
- MOTES as a chiral derivatizing agent.

3.1. Synthesis of the MOTES group

The synthesis of both enantiomers of MOTES-H (**69**) is straightforward and has already been developed by *Trzoss* in the course of his PhD research.[58] However, following this procedure, we encountered several unexpected problems. While racemic phenylsilane **70** was readily accessed on the given path, the substitution of the phenyl group by the *H*-atom proved problematic and asked for a closer investigation and for optimization of the protocol.

For the preparation of phenylsilane **70**, commercially available triphenylmethane (**73**) was deprotonated by reaction with BuLi and treated with formaldehyde to afford, after subsequent oxidation with pyridinium chloro chromate (PCC), triphenylacetaldehyde (**75**). This aldehyde was reacted, as described earlier, with (dimethyl)phenylsilyllithium (**76**)[60, 61] to afford an alcohol, which was directly methylated by exposure to Me_2SO_4. In contrast to the protocol of *Trzoss*, purification of **70** and **75** was performed by crystallization rather than chromatography, which was more appropriate for the larger amounts of material needed for our investigations. As optimal sovent for the recrystallization of **70** turned out to be a

mixture of hexane/EtOAc (50:1), and phenylsilane **70** was finally obtained by this procedure in overall 75% yield (Scheme 24).

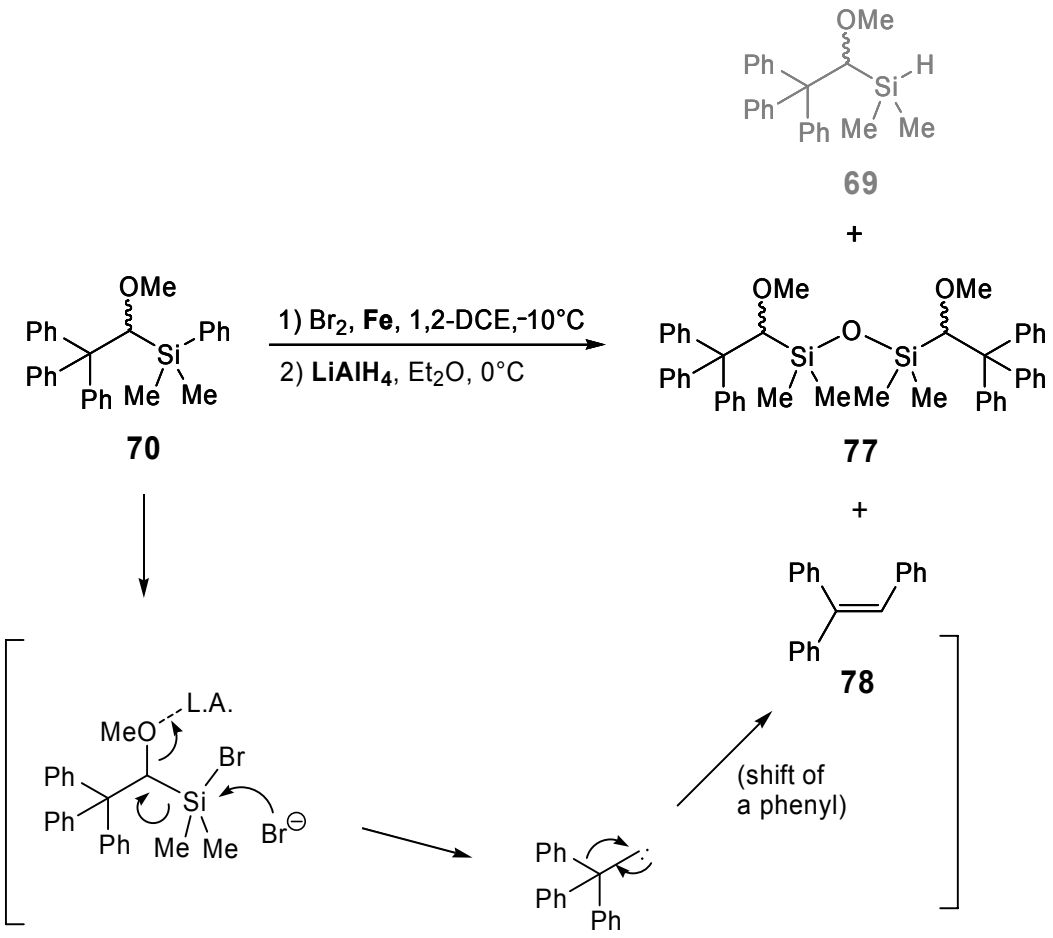


Scheme 24

As already mentioned above, the conversion of phenylsilane **70** into hydrosilane **69** proved more problematic than anticipated. While in some cases the results of *Trzoss* of bromination and subsequent reduction of **70** were easily reproduced, some other attempts failed completely: more often than not, siloxane **77** and/or triphenylethene (**78**) were obtained instead — or in substantial amounts aside — of the desired hydrosilane **69**.

The reasons for the erratical reaction course were not evident. The formation of siloxane **77** suggested the presence of water, and the production of triphenylethene (**78**) could be explained by an acid-catalized process as shown in Scheme 25. Rigorous exclusion of water, particularly from commercially available Br_2 by its treatment with *oleum* (H_2SO_4/SO_3), proved in fact advantageous, but still substantial amounts of siloxane **77** — and particularly still **78** — was found in the product mixtures. It finally turned out that the success of the conversion of **70** into **69** is crucially dependent on two factors: on the quality of the commercial $LiAlH_4$ used for

the reduction of the intermediary bromosilane and on the amount of Fe used in the first step of the transformation, in the electrophilic aromatic substitution of the silyl moiety at the phenyl group.



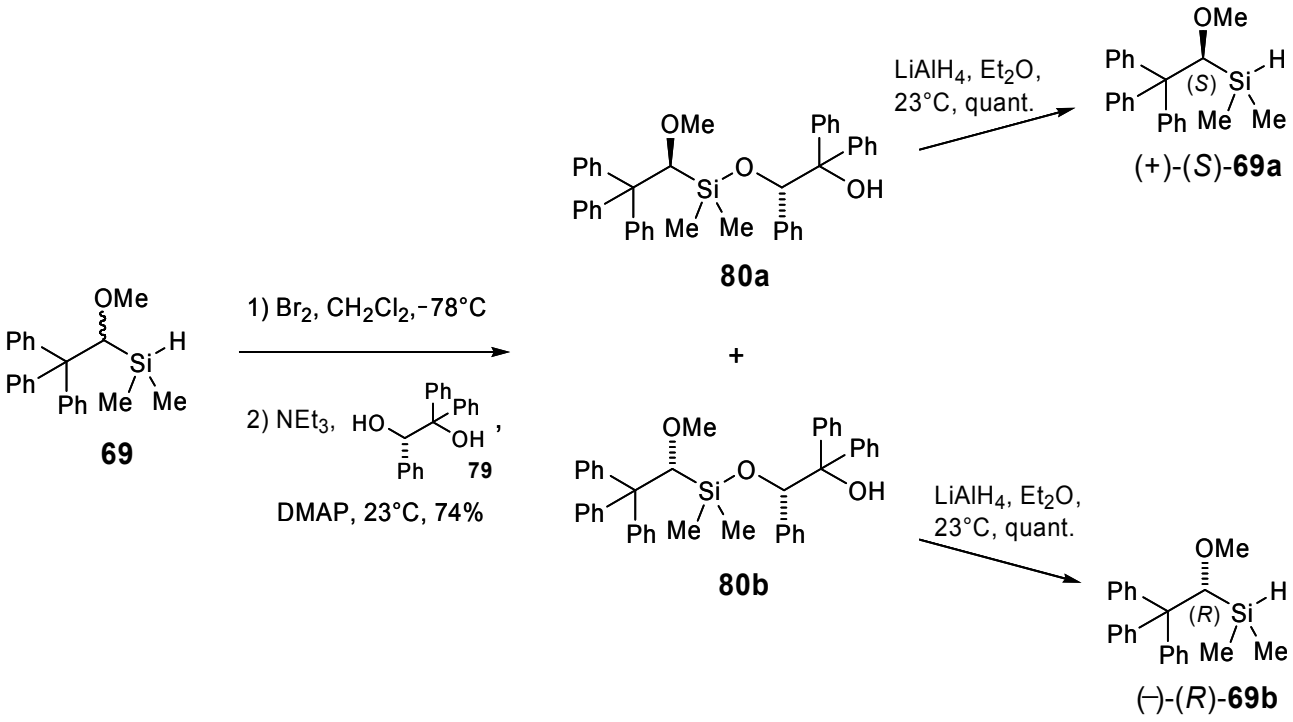
Scheme 25

Assuming that triphenylethene (**78**) was arising along the reaction path shown in Scheme 25, its formation should strongly be dependent on the acid content ($FeBr_3$) of the reaction mixture. We thus performed a row of experiments where the amount of Fe, added to the mixture in the first step of the sequence, was varied, and we found that an added Fe-amount exeeding 8% caused inherently the formation of the undesired product **78**. After learning that commercial $LiAlH_4$ contains up to 10% of impurities, of which Fe is the major constituent, we started to understand why we

experienced that the success of the transformation was also strongly dependent on the batch of $LiAlH_4$ used.

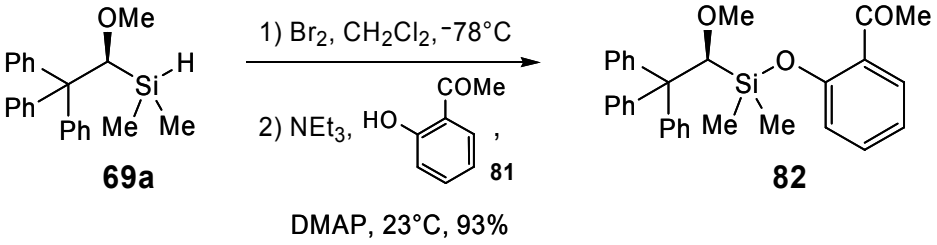
In the final procedure we used 5% of Fe-additive in the first step of the transformation and performed the reduction in the second step with a commercial solution of $LiAlH_4$, the quality of which proved more reliable than that of solid $LiAlH_4$ powders. We still regard it as advisable, however, to test the quality of the $LiAlH_4$ in a small-batch transformation prior to run a big-scale reaction.

For the resolution of the enantiomeric hydrosilanes (+)-(*S*)-**69a** and (–)-(*R*)-**69b**, the original protocol of *Trzoss* could again be followed (Scheme 26). (*rac*)-**69** was reacted with Br_2 and derivatized with (*S*)-1,1,2-triphenylethane-1,2-diol (**79**) to obtain two diastereomeric silylethers **80a** and **80b**, and separation of of the two compounds was achieved by column chromatography (SiO_2, toluene). Reduction of the separated silylethers with $LiAlH_4$ finally furnished (*S*)- and (*R*)-MOTES-H in enantiomerically pure form (established on the basis of the diasteromeric purities of the ethers **80a** and **80b** exceeding 99.9% de).[58]



Scheme 26

Since the relative configurations of the silyl ethers **80a** and **80b** were not accessible, the absolute configurations of the hydrosilanes (+)-(*S*)- and (–)-(*R*)-MOTES-H ((+)-(*S*)-**69a** and (–)-(*R*)-**69b**) were proven by conversion of (+)-**69a** into crystalline silylether **82** (Scheme 27),[58] which revealed its absolute comfiguration in a single crystal X-ray analysis — the silicon and oxygen atoms representing enough "heavy atoms" to effect anomalous X-ray scattering (Figure 9).



Scheme 27

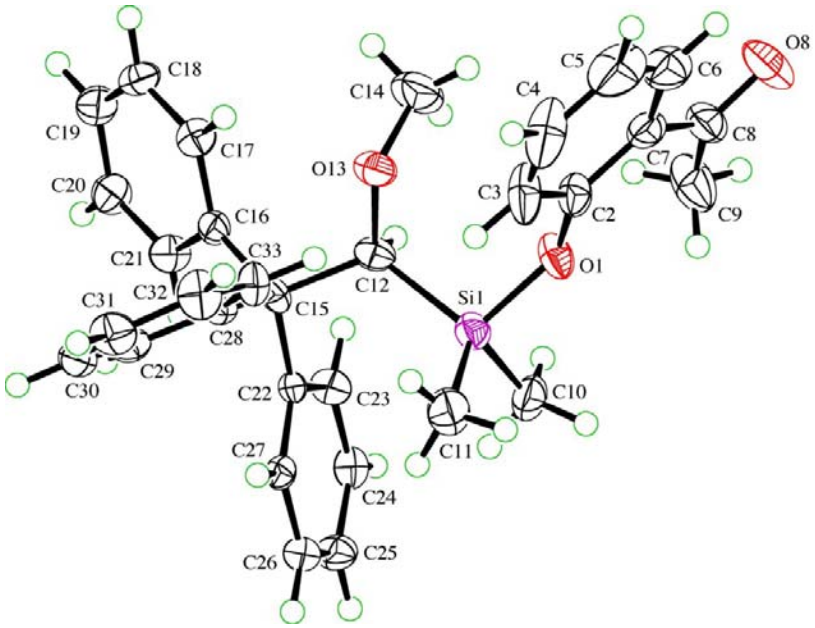
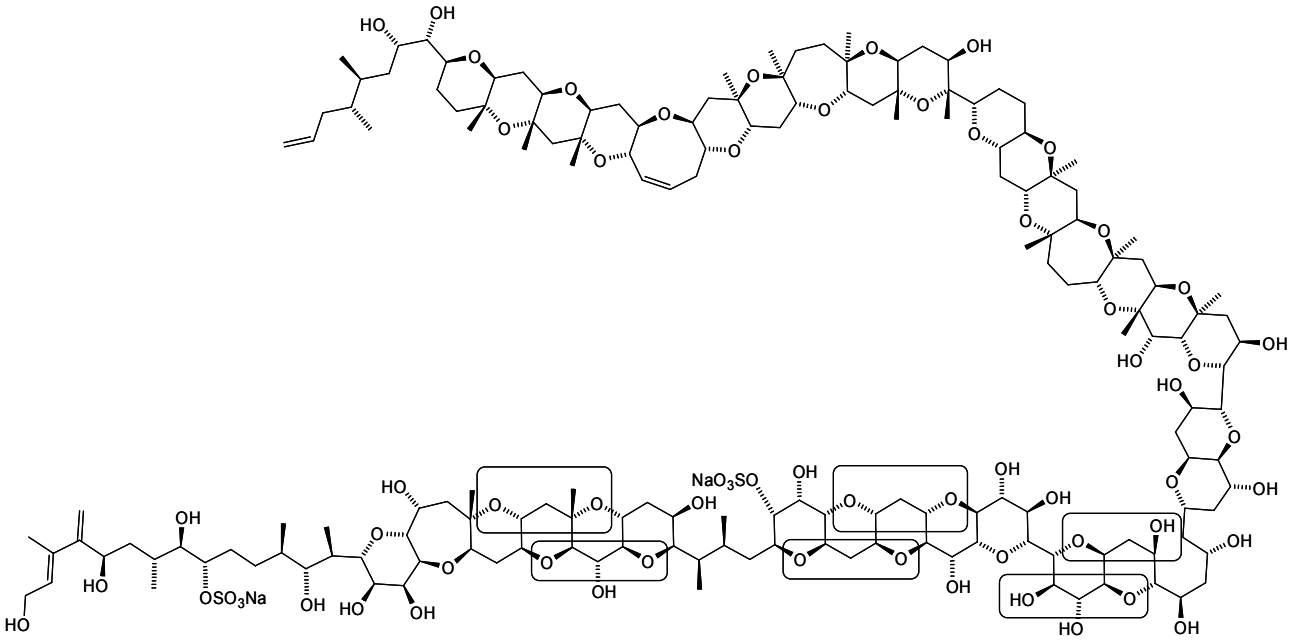


Figure 9. X-ray structure of **82**.[58]

3.2. Stereoselective reactions of silylethers

3.2.1. Motivations

An important class of compounds, being portions of a many — also structurally complex — natural products and bioactive molecules, are the chiral alkane-1,3-diols. For instance polyketide-derived natural products, many of which contain a *syn*- or *anti*-1,3-diol unit, have attracted much attention,[62] particularly because they were shown to represent one of the most potent class of biological active compounds known today. The polyketide maitotoxin (**83**), for example, is the most toxic, non-proteinogenic natural product isolated so far; it contains — among other structural features — a number of 1,3-dioxy moieties as its most repetitive unit (some of which are underlined in Figure 10).[63]

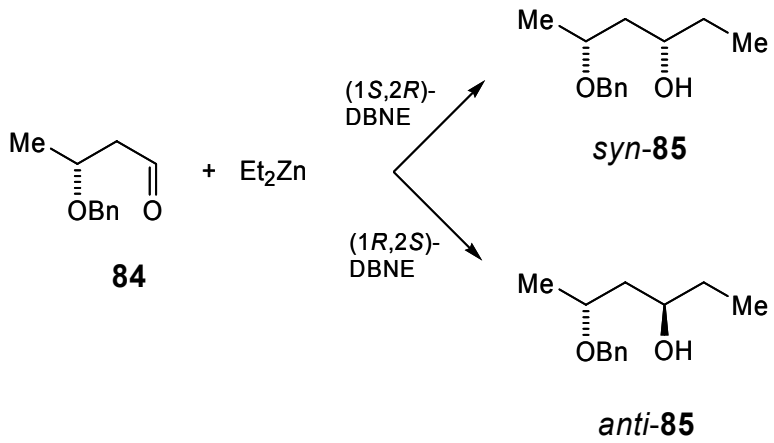


83

Figure 10

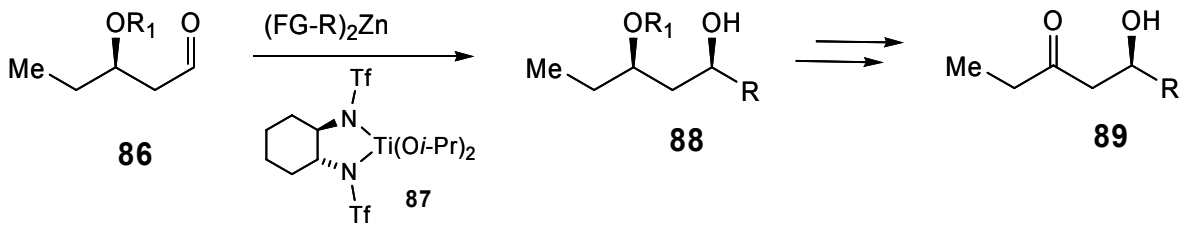
The combination of highly specific biological activity and broad structural diversity is challenging for synthetic chemists. Yet, nature has developed a flexible and iterative approach for the synthesis of the 1,3-dihydroxy motive using only a few building blocks —like acetate, malonate, propionate, or butyrate — for construction of a the broad structural diversity. Since chemists are still not able to follow nature's general approaches for the flexible synthesis of such natural products, a *plethora* of other methods for the stereoselective synthesis of 1,3-diols had and still has to be developed: asymmetric homogeneous and heterogeneous hydrogenations and diastereoselective reductions, chain elongations by radical mechanisms, enzymatic and non-enzymatic desymmetrizations, and dynamic kinetic resolutions, to mention just a few. Far more than 1000 publications appeared over the last 15 years dealing with aspects of the stereoselective synthesis of 1,3-diols. Among these, organozinc reagents have been efficiently used by *Yamashita* et *al.* for the stereoselective synthesis of optically active *syn*- and *anti*-1,3-diols by alkylation of a

β-alkoxyaldehyde in presence of chiral ligands as catalysts.[64] When (*R*)-3-benzyloxybutanal (**84**) was treated with diethylzinc using (1*S*,2*R*)- or (1*R*,2*S*)-(–)-*N,N*-dibutylnorephedrine (DBNE) as a chiral catalyst, *syn*- or *anti*-**85** were obtained in 43% yield with 78% de (Scheme 28). The stereochemical outcome of the reactions was thus not controlled by the stereogenic center of the substrate but rather by the structure of the catalyst.



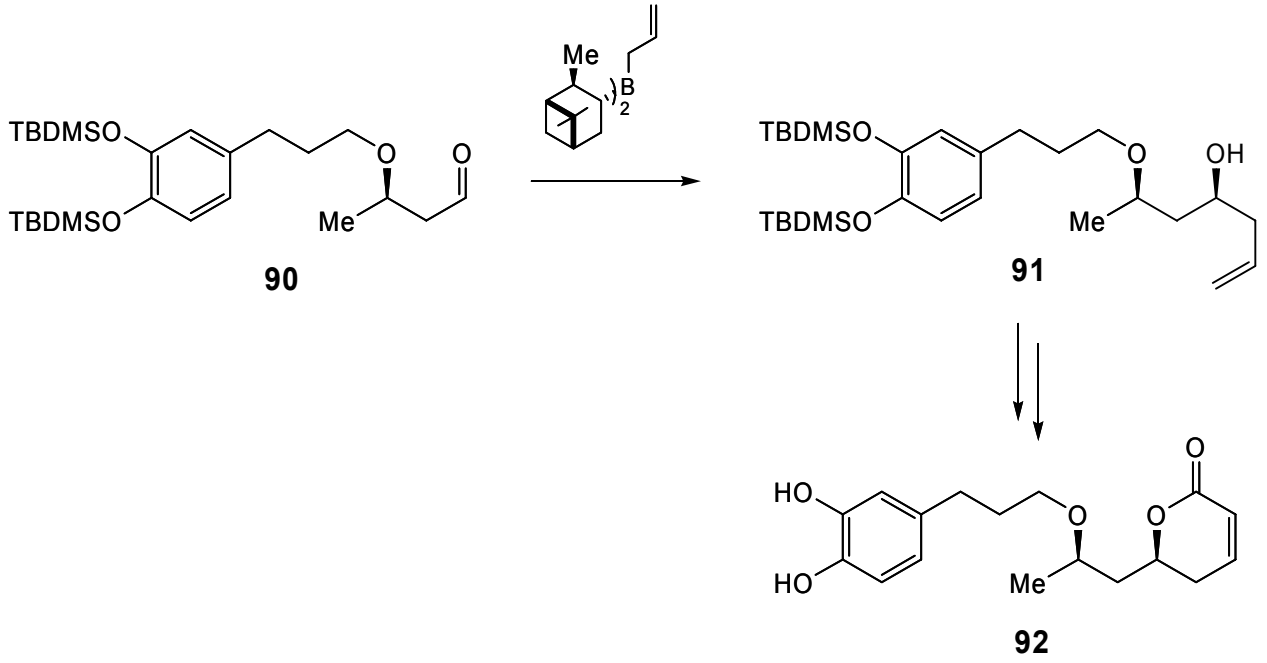
Scheme 28

A variation of the reaction of *Yamashita*, the stereoselective addition of functionalized dialkylzincs catalyzed by chiral *Lewis* acids, developed by *Knochel et al*., has been applied to the stereoselective synthesis of both *syn*- and *anti*-1,3-diols, like in the addition of bis(4-acetoxybutyl)zinc to β-alkoxyaldehydes **86** in presence of titanium catalyst **87** (87% yield, *syn/anti* up to 86:14).[65] Since both enantiomeric forms of the catalyst **87** are readily available and the reaction is mainly under catalyst control, this method allows, in principal, the preparation of both enenatiomeric 1,3-diols (Scheme 29).



Scheme 29

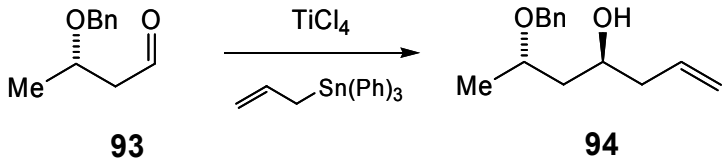
Brown's auxiliary-induced methodology of allylboration of aldehydes[66] was applied by *Ramachandran* and coworkers in the asymmetric synthesis of tarchonanthuslactone (**92**) (Scheme 30).[67] The coordination of boron ensures a high rigidity of the transition structure, which is responsible for the 97% de — arising reagent-controlled — observed in this reaction.



Scheme 30

Another example of excellent stereocotrol in allylation reactions is offered by *Keck* and *Murry*, who applied the known titanium tetrachloride promoted allylation of allylstannanes to an appropriately protected chiral aldehyde such as **93** to give the *anti*-homoallylic alcohol **94** in 75% yield (*anti*:*syn* 29:1) (Scheme 31).[68] The

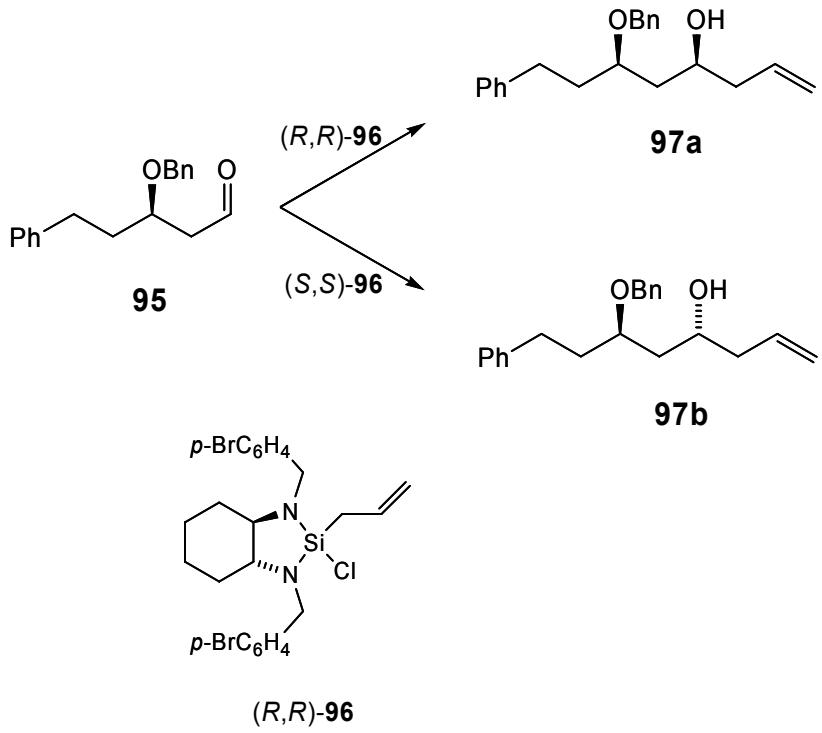
stereoselectivity of this reaction can be explained by the extended chelate model of *Cram*.[69, 70]



93 **94**

Scheme 31

New methodologies and modifications of known procedures applicable to the stereoselective synthesis of 1,3-diols emerge frequently. *Leighton* and *Kubota*, for example, developed strained chiral silacycles like **96** as reagents for selective allylation of aldehydes.[71] These transformations were achieved with diastereoselectivities of up to 96% (Scheme 32).



Scheme 32

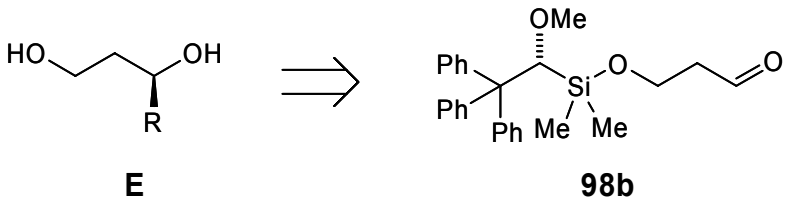
As can be seen, all these methods for the preparation of 1,3-diols are based on stereoselective nucleophilic additions to β-hydroxyaldehdes. Most of the procedures

require initially the protection (in some cases with a silicon group) of the free hydroxyl function, while a chiral metal catalyst or auxiliary is needed to effect stereoselectivity in most cases. Finally, at the end of the reaction sequence, derivatization of the product with a CDA is necessary for the establishment of absolute configurations and the enantiomeric excesses (typically *Mosher* esters are prepared and analyzed).

In the following we will show that the MOTES group can be efficiently used for the stereocontrolled synthesis of enantiomerically enriched 1,3-diols through nucleophilic additions to β-silyloxyaldehydes.

3.2.2. Stereoselective nucleophilic additions to MOTES-derivatized β-silyloxy aldehydes

Motivated by the promising results obtained by *Trzoss* in MOTES-controlled stereoselective additions to α-silyloxyaldehydes,[58] we tried to extend the method to the synthesis of 1,3-diols through nucleophilic additions to MOTES-derived β-hydroxy carbonyl compounds.[72, 73] We were particularly interested to see whether or not chiral 1,6-induction could be made operative and if yes, to which extent enantiomeric excesses of chiral 1,3-diols of type **E** can be obtained (Scheme 33).



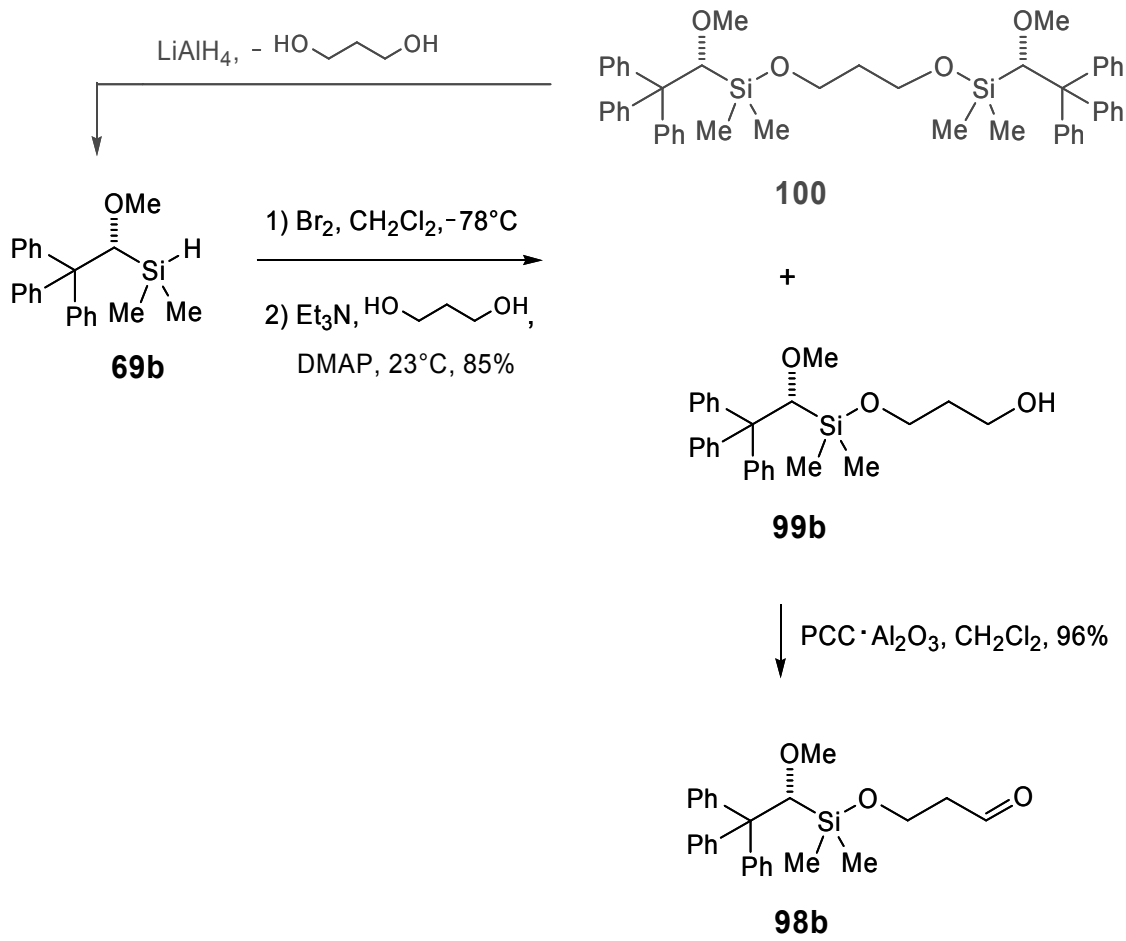
E **98b**

Scheme 33

Since β-hydroxyaldehydes are not commercially available, we decided to prepare the desired carbonyl compound from **69b** and propane-1,3-diol (Scheme 34).

Bromination of (*R*)-MOTES-H (**69b**), followed by addition of propane-1,3-diol, afforded silylether **99b** in good yield, the major side product being the double-protected silylated propane-1,3-diol **100**. The formation of **100**, however, was minimized by use of a larger excess of the diol, and the side product still obtained with this optimized procedure was readily re-converted into **69b** by reduction with $LiAlH_4$.

More problematic than the mono-silylation of propane-1,3-diol proved the subsequent oxidation of alcohol **99b** to the desired aldehyde **98b**. The most common procedures used for the oxidation of primary alcohols to aldehydes — *Swern*-oxidation or variations thereof as well as oxidations with with PCC (pyridinium chloro chromate) — failed completely or afforded the desired (*R*)-3-propionoxyaldehyde (**98b**) in very low yields only. Substantial decomposition probably due to a β-elimination of the product to silanol and (possibly) acrylaldehyde occurred. However, reaction with a solution of NaOCl and TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl), and particularly with PCC adsorbed on basic alumina provided the desired aldehyde **98b** in high yields (Scheme 34).

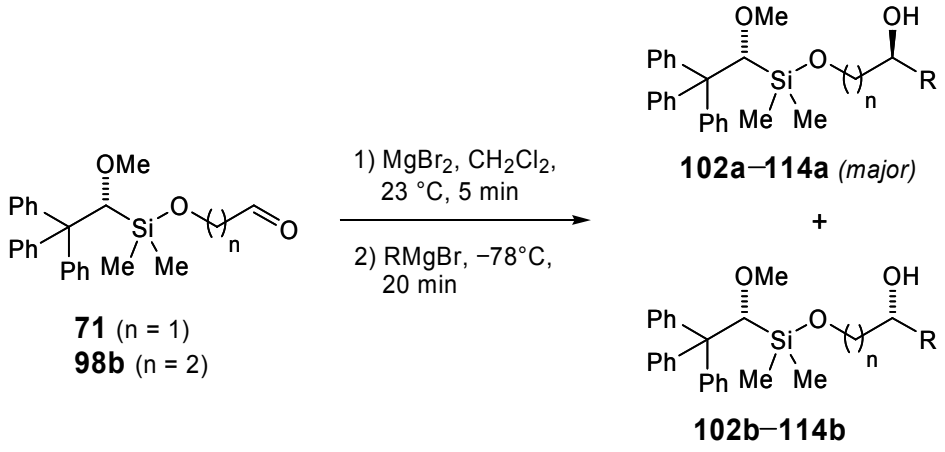


Scheme 34

The MOTES-derivative **98b** was then treated in CH_2Cl_2 at –78 °C with $MgBr_2$ as a *Lewis* acid to ensure chelation,[59] before it was reacted with a number of *Grignard* reagents. The results of these transformations are summarized in Table 1 — for reason of comparison together with the results obtained by *Trzoss* in his analogous *Grignard* additions to the MOTES-derivative of α-hydroxyacetaldehyde **71**.[58] The selectivities that were obtained with β-silyloxyaldehyde **98b** were consistently lower than those obtained with the related α-silyloxyderivative **71**. However, diastereomeric ratios of as high as 16:1 — except for the reaction with the sterically unconstrained ethynyl-*Grignard* reagent — are still among the best found for chiral 1,6-inductions so far.[74] The product ratios of mixtures **108**–**114** were determined by ^{1}H-NMR through integration of characteristic peaks — typically the singlets

deriving from the Me_2Si groups — and confirmed later, on the stage of the MTPA-derivatized alcohols **115–120** (see Experimental part, section 5.3), by analysis of their ^{1}H-NMR and ^{19}F-NMR spectra.

Table 1. Results of MOTES-directed addition reactions.



71 (n = 1)
98b (n = 2)

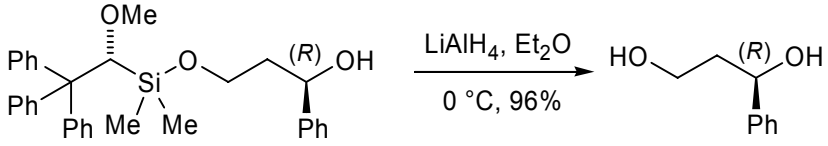
102a–114a *(major)*

102b–114b

Entry	Educt	n	Reagent	Product	R	Yield	*dr*
1	**71**	1	MeMgBr	**102a–102b**	Me	97	70:1
2	**71**	1	EtMgBr	**103a–103b**	Et	95	80:1
3	**71**	1	*i*-PrMgBr	**104a–104b**	*i*-Pr	93	70:1
4	**71**	1	PhMgBr	**105a–105b**	Ph	96	70:1
5	**71**	1	AllylMgBr	**106a–106b**	Allyl	88	80:1
6	**71**	1	VinylMgBr	**107a–107b**	Vinyl	91	70:1
7	**98b**	2	MeMgBr	**108a–108b**	Me	96	14:1
8	**98b**	2	EtMgBr	**109a–109b**	Et	95	15:1
9	**98b**	2	*i*-PrMgBr	**110a–110b**	*i*-Pr	96	11:1
10	**98b**	2	PhMgBr	**111a–111b**	Ph	91	12:1
11	**98b**	2	AllylMgBr	**112a–112b**	Allyl	98	16:1
12	**98b**	2	VinylMgBr	**113a–113b**	Vinyl	93	16:1
13	**98b**	2	EthynylMgBr	**114a–114b**	Ethynyl	97	1:1

[a] Combined yields of the two isomers.

As support of the informations obtained after derivatization of the reaction mixtures with *Mosher* chloride, the absolute configuration of compound **111a** was unambigously confirmed by chemical correlation. **111a** was separated on preparative TLC from **111b** and subsequently reduced with $LiAlH_4$ to afford (*R*)-MOTES-H and (+)-1-phenylpropane-1,3-diol (**121**). Comparison of the optical rotation of (+)-**121** ($[\alpha]_D^{25}$ = +66.3 (c = 0.90, $CHCl_3$)) with the value reported in literature ((*R*)-**121**: $[\alpha]_D^{25}$ = +69.0 (c = 1.00, $CHCl_3$)),[75, 76] confirmed the (*R*) configuration at the stereogenic center (Scheme 35)



111a **121**

Scheme 35

The stereochemical outcome of the reactions is consistent with the formation of an intermediary tridentate chelate complex as shown in Figure 11, where the π-facial attack is sterically controlled. It was experienced that the *Lewis* acid plays a pivotal role with regard to the extent of the selectivities — without pre-complexation of the substrates, distinctively lower selectivities were observed for all transformations.

On first sight, the proposed transition structure might appear disadvantageous due to the positioning of the demanding trityl group on the *endo*-site of the bicyclic system. However, the trityl group adopts a *pseudo*-equatorial position in the envelope-shaped five-membered ring avoiding unfavorable interactions with the *pseudo*-axially positioned Br- and the H-atoms.

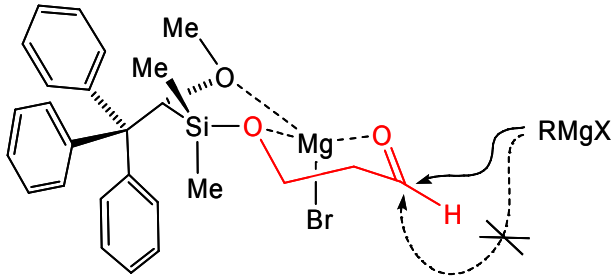


Figure 11. Proposed *Mg*-complex in the transition structure.

An application of the addition of organometallics to MOTES-derivatized β-hydroxy carbonyl compounds is shown with the enantioselective synthesis of naturally occurring octane-1,3-diol (**122**) (Figure 12).[77] In 1973, octane-1,3-diol was identified as a natural constituent of apples, and some years later, further octanediol derivatives, such as (*Z*)-oct-5-ene-1,3-diol (**123**), were reported as constituents of *Kogyoku* apples,[78] *Rheinischer Bohnapfel*, *Purpurroter Cousinot* and *Börtlinger Weinapfel*.[79] Both diols **122** and **123** are considered to be intermediates of fatty acid methabolism, and radiolabeling studies indicated that linoleic acid and linolenic acid were the natural precursors of **122** and **123**, respectively.[80]

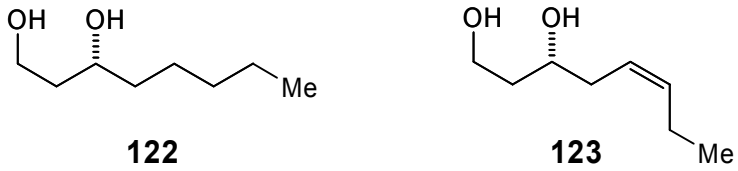
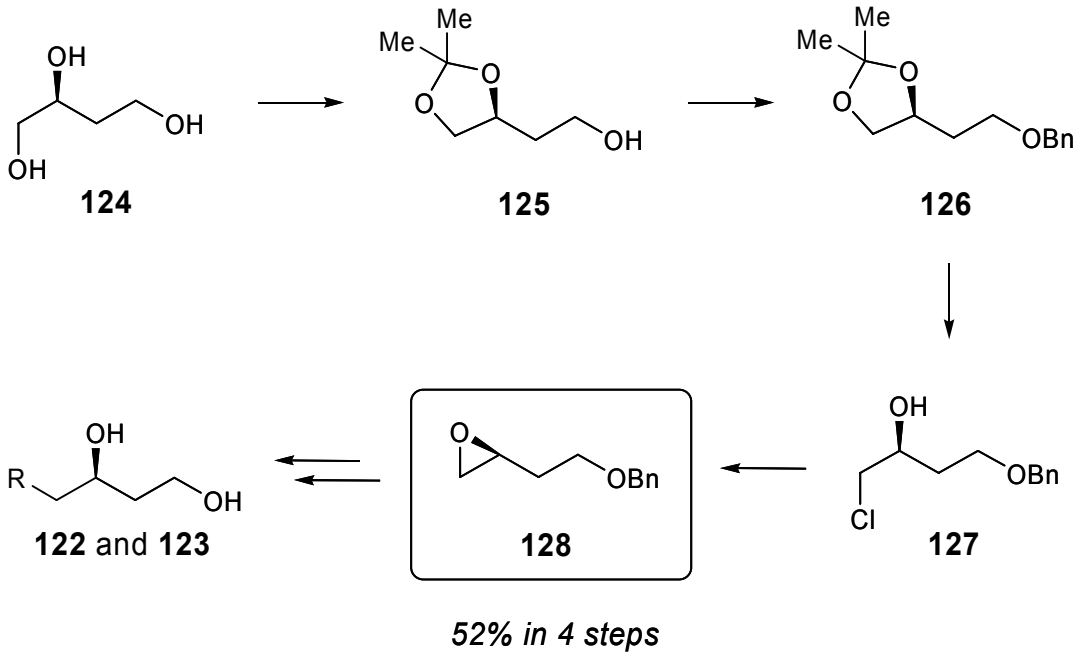


Figure 12

In 1974, diol **122** was patented for its antimicrobial effects as a food additive for fish, chicken, beef, and eggs as well as for dairy products including butter and milk. The diol is effective in controlling the reproduction of microorganisms associated with infections in humans and animals.[81] Raw grain, feed compositions, and intermediate moisture food compositions such as apple flakes show great resistance to the attack of molds, bacteria, and yeast when prepared with **122**.[82, 83] This diol is

harmless to humans at high concentrations and exhibits antimicrobial effects, being easily resorbed and metabolized.

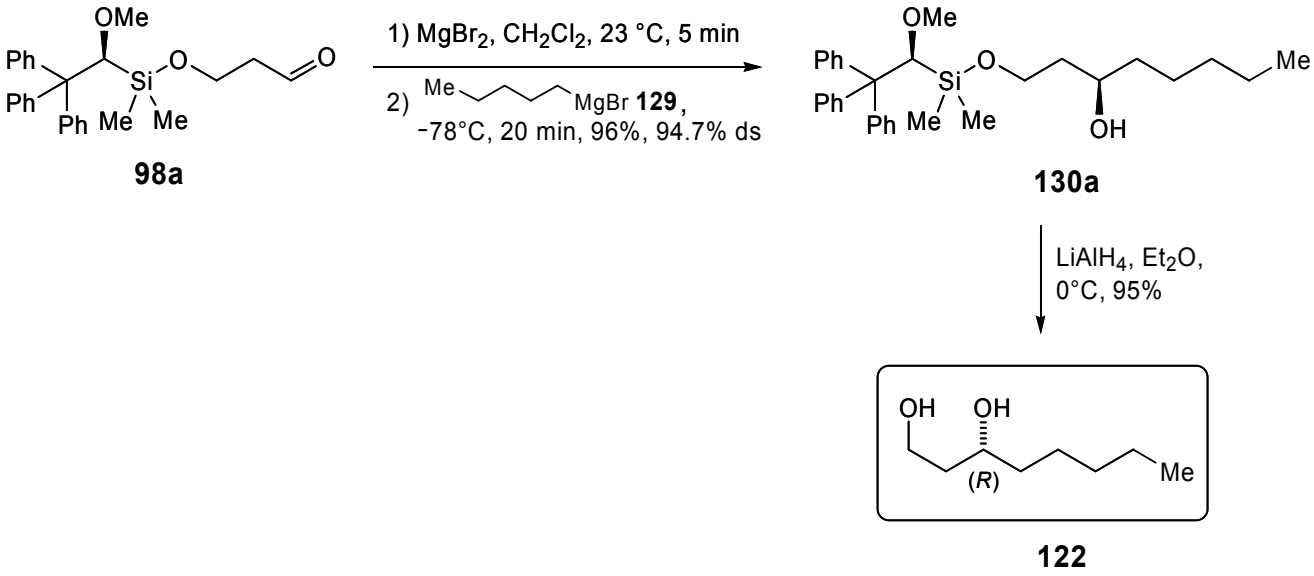
Despite a conspicuous number of possible ways suitable for the preparation of the diols **122** and **123**, the most efficient routes to synthesize **122** in enantiomerically pure form are still based on the opening of *O*-benzyl-protected epoxide **128** as shown in Scheme 36. Even though the preparation of **128** from **124** is rather laborious and finally low yielding, it seems still more satisfactory than the direct asymmetric epoxidation of the corresponding but-3-en-1-ol.[84]



Scheme 36

To access diol **122**, the MOTES-directed addition of pentyl magnesium bromide to **98a** (obtained from **69a** by following the same procedure used for the preparation of **98b**) thus appeared to be a straightforward and attractive alternative. Hence, compound **98a** was treated in CH_2Cl_2 with $MgBr_2$ at –78 °C, and 1-pentyl magnesium bromide (**129**) in Et_2O was added dropwise to the solution (Scheme 37). After workup, alcohol **130a** was obtained with 96% yield and 94.7% *ds*, determined

by ^{1}H-NMR through integration of the singlets deriving from the Me_2Si groups of the two isomers. Compound **130a** could be easily separated from **130b** by preparative thin layer chromatography and finally reduced with $LiAlH_4$ to deliver (*S*)-MOTES-H **69a** and the enantiopure 1,3-diol **122** in 95% yield. The absolute configuration of the product was established by comparison of the optical rotation of **122** ($[\alpha]_D^{25} = -9.1$ (c = 1.50, $CHCl_3$)) with the one reported in literature ((*R*)-**122**: $[\alpha]_D^{25} = -11.2$ (c = 1.32, $CHCl_3$)).[85]

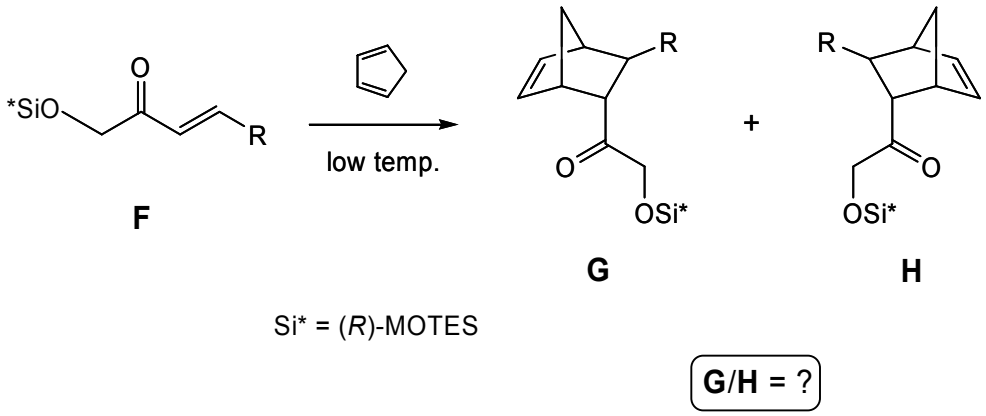


Scheme 37

3.2.3. Diels–Alder reactions

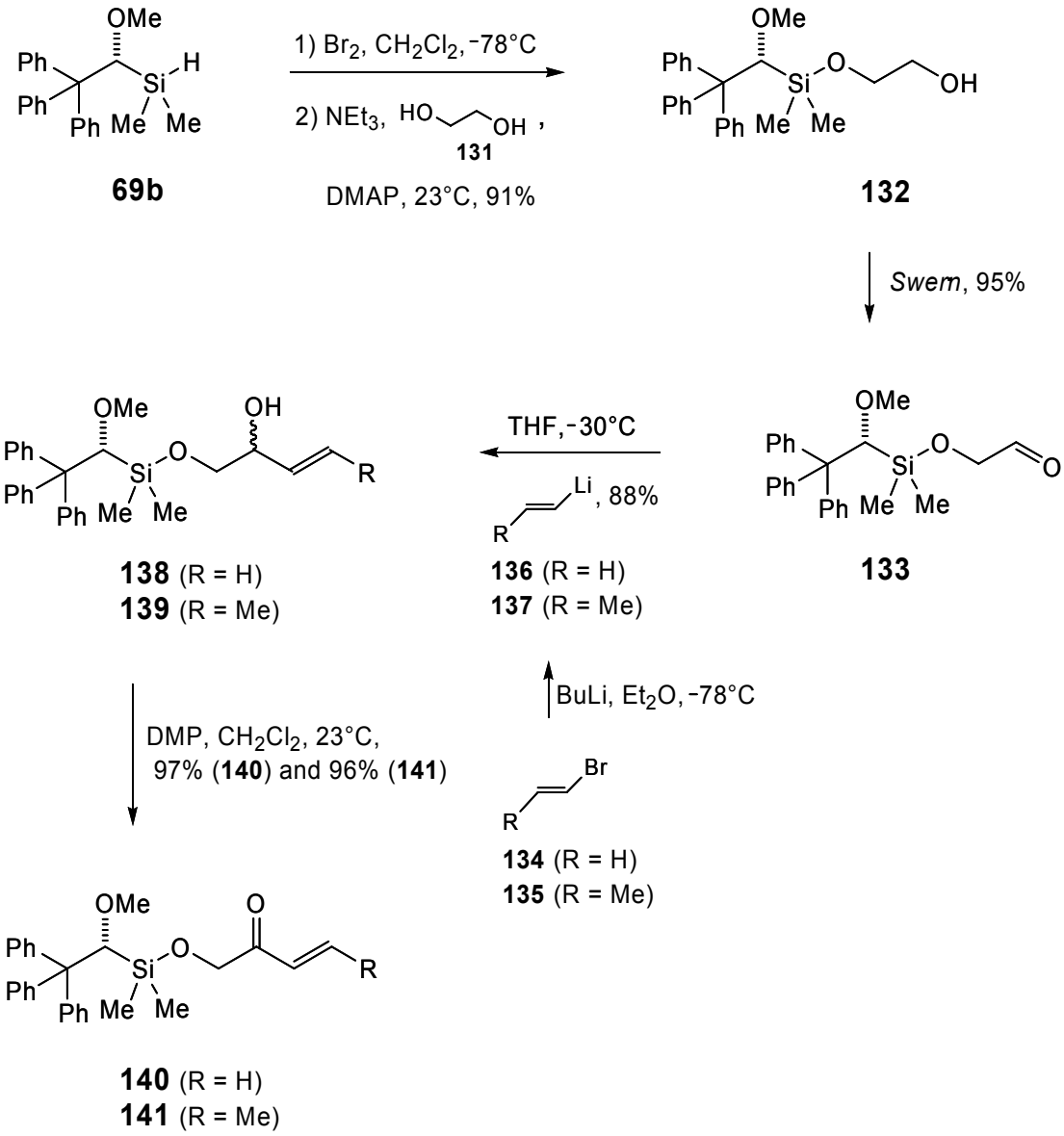
Since the chelate-controlled additions of organometallics to MOTES-derivatized α- and β-hydroxycarbonyl compounds proved successful, proceeding with good yields and high degrees of stereoselectivity, we tried to extend the application of MOTES to other stereoselective processes. MOTES-derivatized α-hydroxy-α',β'-unsaturated carbonyl compounds appeared to be suitable substrates for *Diels–Alder* reactions: they should form similar chelate complexes as the already investigated silylated hydroxyaldehydes and thus preferrably exhibit one of the two π-faces to a diene in a [4+2] cycloaddition.

As known for already a long time, *Lewis* acid-catalyzed *Diels–Alder* reactions proceed with high *endo*-selectivities, substantially higher than those of the non-catalyzed versions.[86] The chelate-controlled *Diels–Alder* reaction of the MOTES derivatives of type **F** with dienes such as cyclopentadiene was thus expected to proceed with high stereocontrol, not only with regard to the π-facial selectivity but also with respect to the *endo*-selectivity. In the case of use of the (*R*)-MOTES derivatives **69b**, the [4+2] cycloadditions were expected to lead preferentially to products of type **G** under conditions of kinetic control (Scheme 38).



Scheme 38

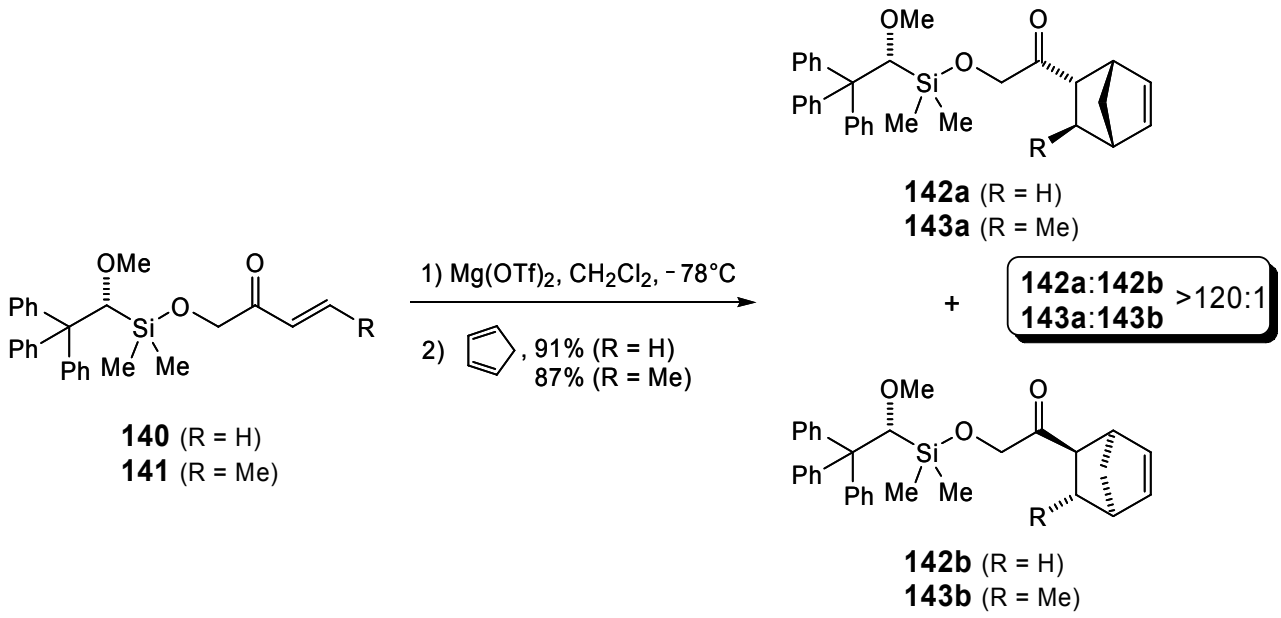
The α-silyloxy-α',β'-unsaturated ketones **140** and **141** needed for the intended *Diels–Alder* reactions were readily prepared as illustrated in Scheme 39. Bromination of (*R*)-MOTES-H (**69b**) followed by addition of ethane-1,2-diol (**131**) afforded silylether **132**, which was oxidized with PCC adsorbed on basic alumina to the correspondent aldehyde **133**.[58] Alcohols **138** and **139** were subsequently obtained by reductive alkylation of aldehyde **133** with vinyl (**136**) and propenyllithium (**137**), respectively (prepared from the correspondent bromides **134** and **135**), and their oxidation with Dess-Martin periodinane (DMP) gave ketones **140** and **141**.



Scheme 39

The *Diels–Alder* reactions were performed with the two α,β-unsaturated ketons **140** and **141** at –78 °C (Scheme 40). After pre-complexation of the dienophiles with $Mg(OTf)_2$, the substrate was allowed to react with cyclopentadiene, which was added in excess. As expected, the cycloadditions proceeded with high stereoselectivities: in fact, exclusively the two diastereomeric *endo*-isomers were detected, and their ratio was found to be higher than 120:1 for the products of both reactions (the limit of detection being given by the sensitivity of the NMR measurements). In order to

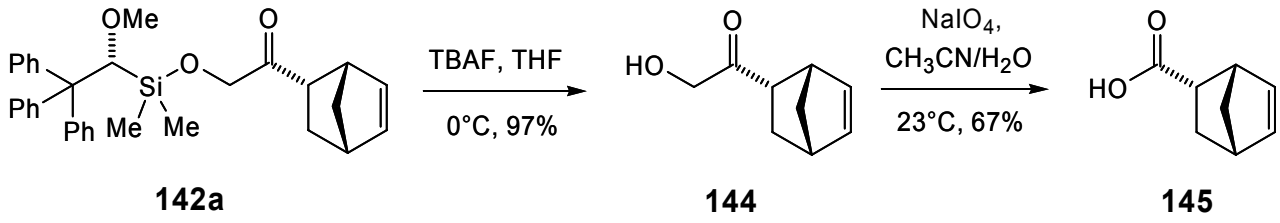
localize and identify the signals of both isomers — to be sure that the two isomers are in fact distinguishable by NMR —, a intentionally less selective reaction was performed: treatment of **140** with cyclopentadiene in toluene at 60 °C, without *Lewis* acid catalysis, afforded two products in a ratio of approximately 1:1, which turned out to be the two diastereomeric *endo*-isomers. The Me_2Si signals of these two compounds were clearly distinguished in ^{1}H-NMR.



Scheme 40

The relative configuration of the stereogenic centers in the cycloaddition products could not be directly determined, but, again, the absolute configurations of the newly formed stereogenic units in **142a** and **143a** were deduced by chemical correlation (Scheme 41). This allowed finally the characterization of the stereochemical impact of the MOTES group. Exemplarily, cycloaddition product **142a** was treated with TBAF to remove the chiral silicon group, affording alcohol **144**. This compound was then oxidized with $NaIO_4$ to bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (**145**), which was levorotatory ($[\alpha]_D^{25} = -126.3$ (c = 1.20, $CHCl_3$)) and thus proved to be of the

shown (1*S*,2*S*,4*S*)-configuration (from literature [(1*S*,2*S*,4*S*)-**145**: $[\alpha]_D^{25} = -139.0$ (c = 1.38, EtOH)).[87, 88]



142a **144** **145**

Scheme 41

The stereochemical result is in agreement with our expectations, correlating to the model of the nucleophilic additions to MOTES-derivatized α-hydroxyaldehydes: a tridentate chelate-structure through *Mg*-complexation rigidifies the conformation of the molecule in the transition state, and the attack of cyclopentadiene occurs onto the less hindered face of the *cisoid*-shaped conjugated double bond (Figure 13).

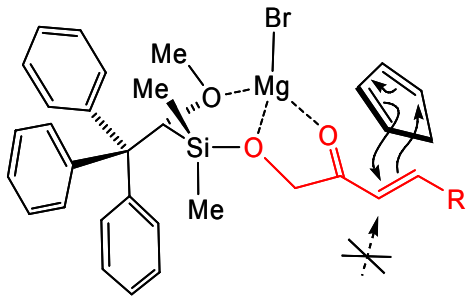


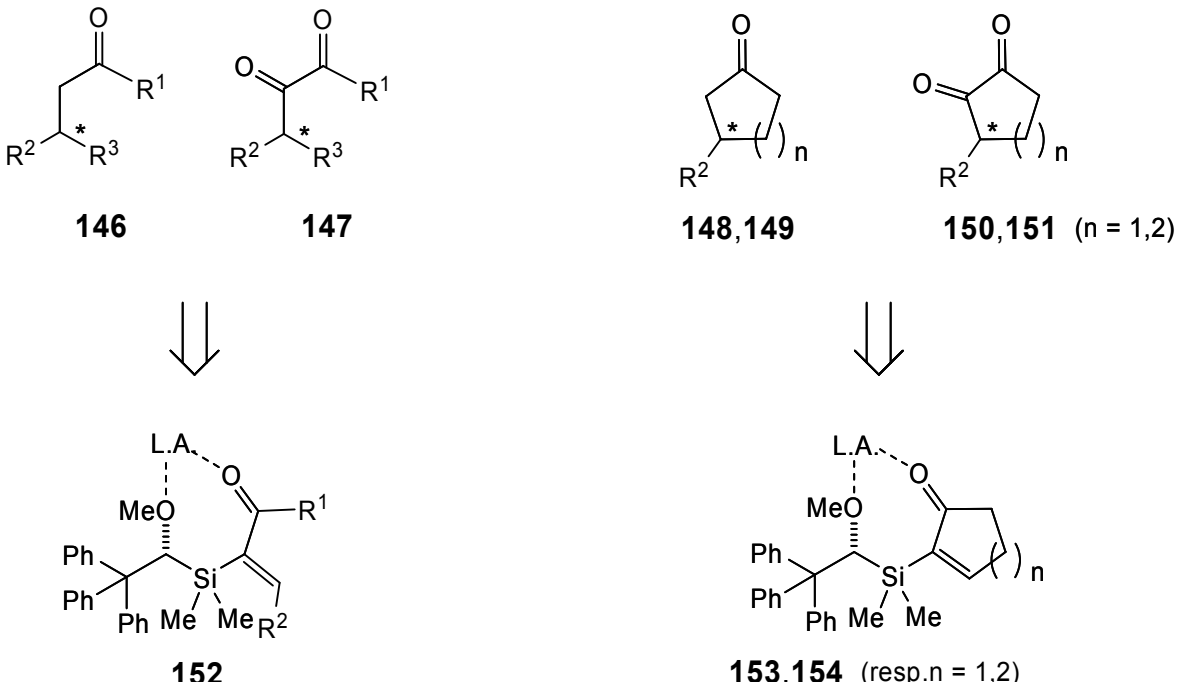
Figure 13. Proposed *Mg*-complex in the transition structure.

Overall, the reactions with MOTES-derivatized α- and β-hydroxy carbonyl compounds have shown that MOTES is a versatile group to be used, concurrently, as protective and efficient stereodirecting group. MOTES-derivatized reaction products can be clearly distinguished by ^{1}H-NMR spectroscopy and a reliable characterization of the reaction mixtures can be effected. Prerequisite for high selectivities seems to be the formation of intermediary rigidified chelate structures (which, in fact, are evidently forced to be formed through addition of *Lewis* acids). At the end of each

transformation, MOTES can be entirely recovered as MOTES-H, after a reductive cleavage with $LiAlH_4$, or as MOTES-F, by treatment with fluoride.

3.3. Reactivity of substrates with MOTES directly linked to the carbon-framework

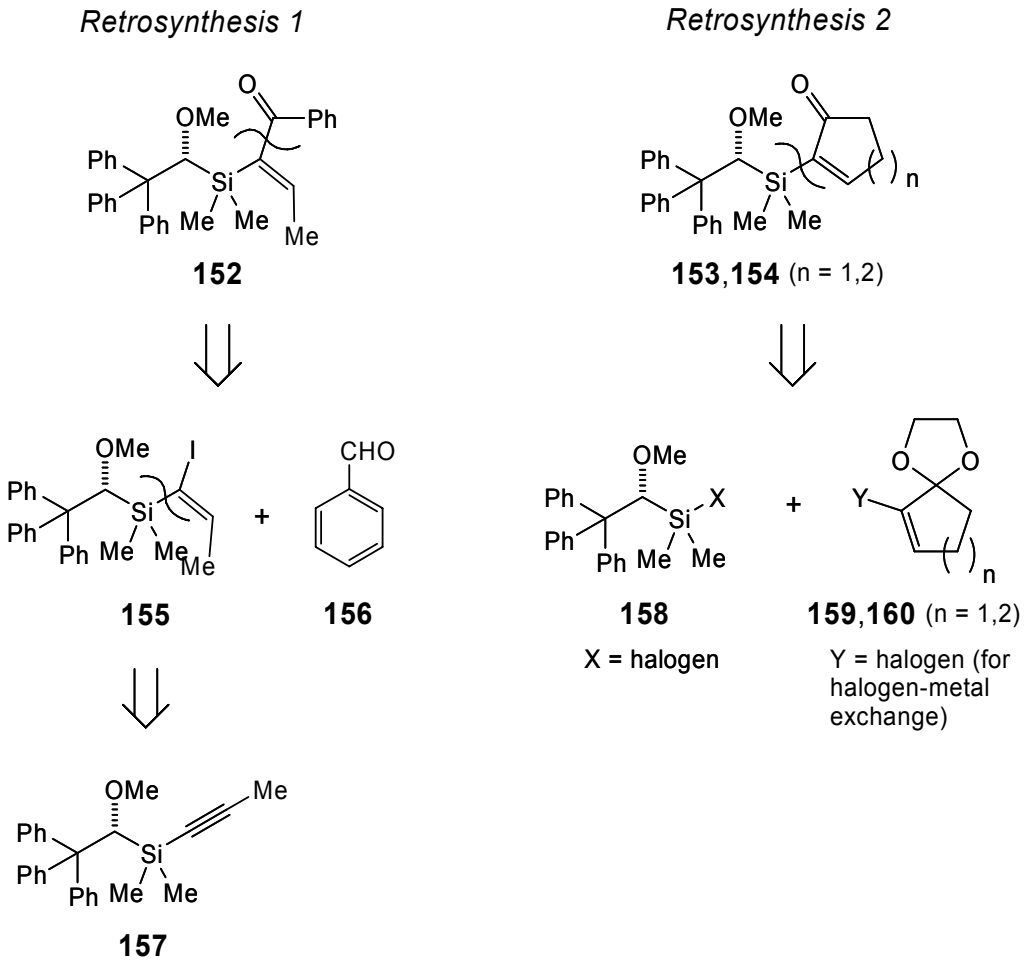
As shown in the introductionary part of this treatise and experienced with earlier investigations of the *Bienz* group, chiral silicon moieties can act as stereochemical directors not only when they are connected to the substrate through an *O*-atom but also (and presumably even more efficiently) when they are connected directly to the carbon framework. In this section we present some results we obtained in the course of our attempts to explore the effect of the MOTES group upon diastereoselective reactions when it is linked directly to the carbon framework. Specifically, we intended to open enantiospecific access to target compounds of type **146**,**147** and **148**–**151** (Scheme 42), known since a while as important building blocks for the synthesis of terpenes, and being investigated since recently as inhibitors of specific enzymes.[89]



Scheme 42

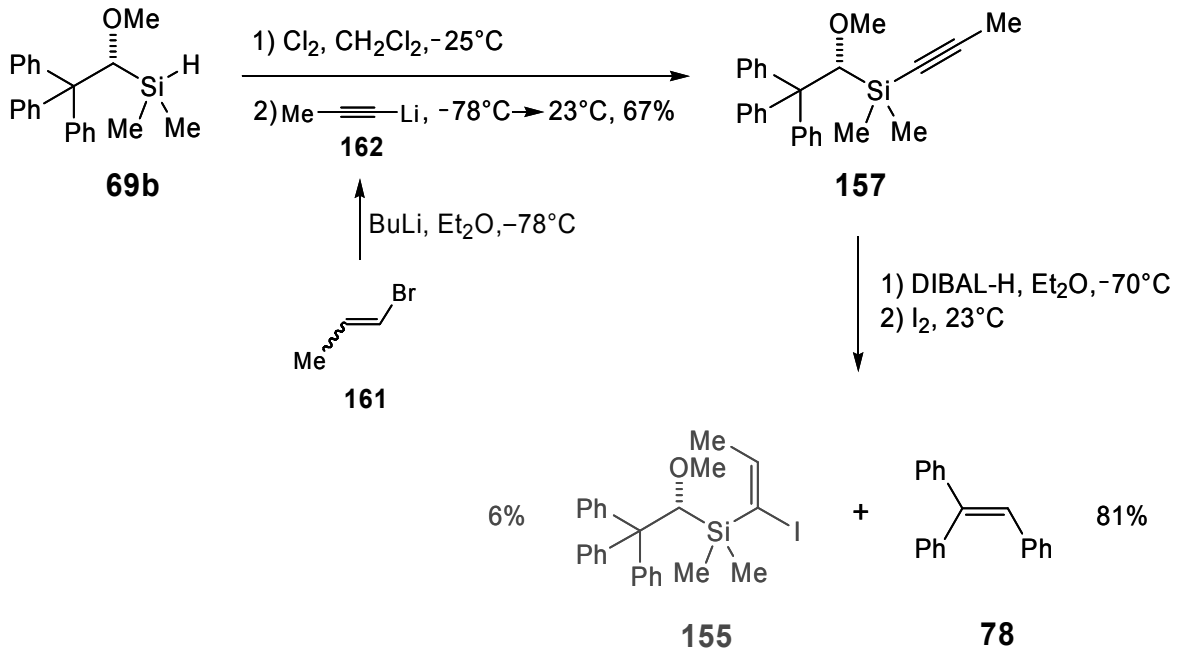
An analysis of these structures reveals a stereogenic center in β-position to a carbonyl group, and such compounds should pricipally be amenable through stereocontrolled *Michael*-type additions, *e.g.*, of cuprates, to appropriate α,β-unsaturated ketones. Relying on the experiences gained with previous investigations of the research collective and the work presented in previous chapters, we were confident that α-MOTES-derivatized α,β-unsaturated ketones **152**–**154** would be suitable substrates to enantiospecifically access products of type **146** and **147** and **148**–**151**; they should be able, in fact, to form rigid chelate transition structures, where the topicity of subsequent transformations would be sterically controlled — as in the previously investigated silylated α- and β-hydroxy carbonyl compounds.

To test the efficiency of MOTES for chelate-controlled cuprate additions to α-silylated α,β-unsaturated ketones, compounds **152**–**154** were envisioned as suitable starting materials. Two different retrosynthetic strategies for the preparation of the two different types of silanes were considered (Scheme 43). The non-cyclic enone **152** could be disconnected, as shown in an analogue example by *Bratovanov*,[90] at the bond between the unsaturated moiety and the carbonyl group, leading retrosynthetically to fragments **155** and **156**, the first of which could be accessible from acetylenic silane **157**. The cyclic counterparts **153** and **154**, however, could derive from precursors of type **158** and **159** or **160**, respectively, through disconnection of the bond between the silyl group and the enone.



Scheme 43

Our investigations started with the attempted synthesis of silane **152**. Starting with (*R*)-MOTES-H (**69b**), the corresponding chlorosilane was prepared *in situ* and treated with propynyllithium[91] (**162**), readily obtained from 1-propenylbromide (**161**) by reaction with BuLi, to deliver silyl acetylide **157** in reasonable yield. Next, the regiospecific *syn*-hydroalumination of **157** with DIBAL-H, followed by oxidative Al–I exchange, was tried to access vinyl iodide **155**. However, despite extensive efforts performed in variation of reaction conditions, compound **155** could be obtained in traces only, as the persistent decomposition product, the old acquaintance triphenylethene (**78**), was constantly isolated as the major component in the product mixture (Scheme 44).

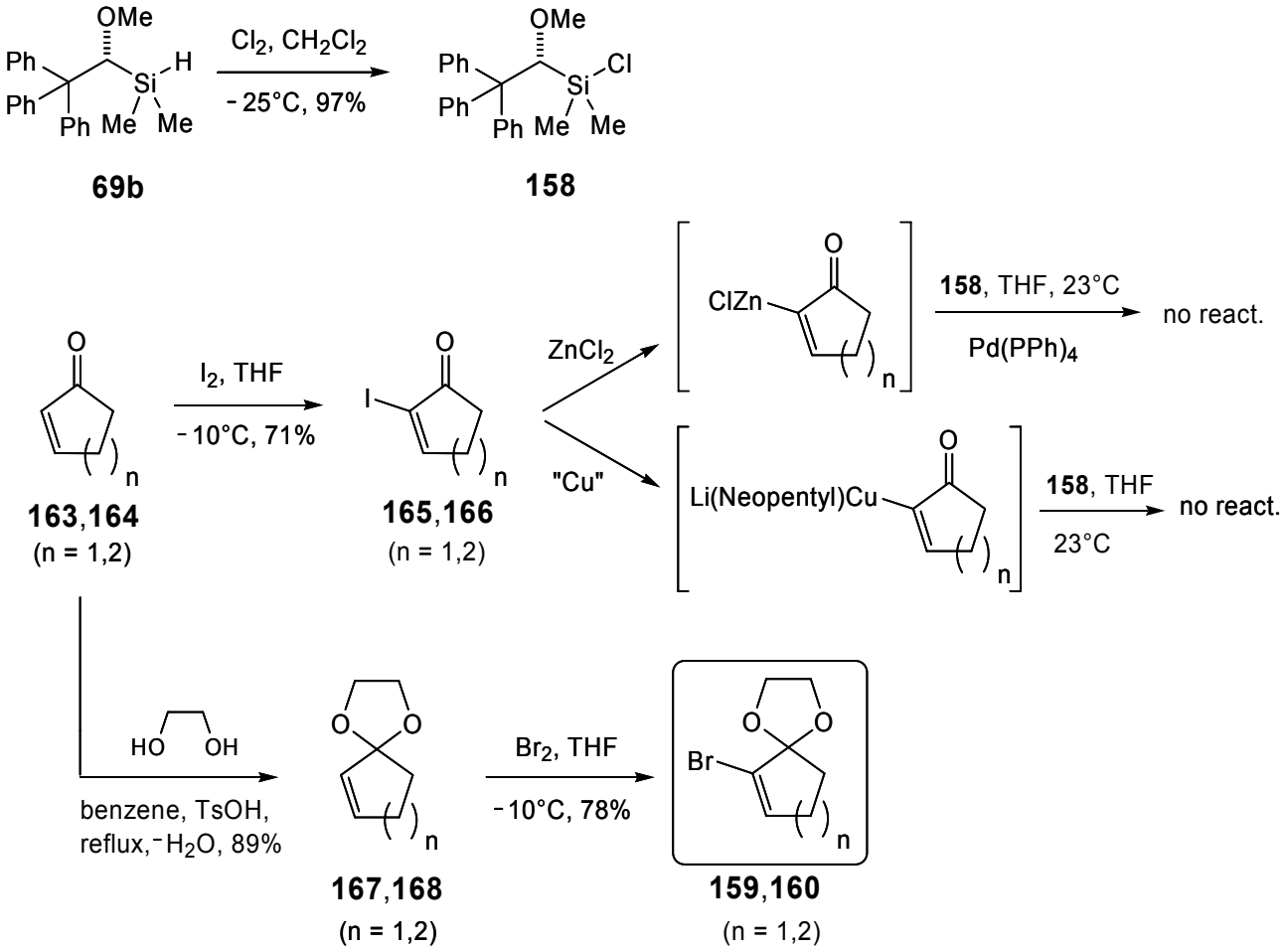


Scheme 44

Since we were not able to prevent the decomposition of the MOTES-moiety in the hydroalumination/iodination step — probably due to the proximity of the *Al*-based *Lewis* acid to the methoxy group — we decided to shift our focus towards the preparation of the cyclic enones **153** and **154**, following the second strategy shown in Scheme 43. On this path, not neccessarily *Lewis* acids have to be involved and thus acid-supported decomposition of the MOTES group should not represent a principal problem. In fact, this proved wrong as will be shown below.

First, chlorosilane **158** was prepared by chlorination of (*R*)-MOTES-H (**69b**). It arose readily as a colorless oil, which could be isolated by distillation and which proved to be stable enough to be stored under Ar at low temperature for a prolonged period of time (Scheme 45). Then, a synthetic route for the preparation of α-metallated enones and enone equivalents was studied. Iodination of enones **163** and **164** by their treatment with elemental I_2 afforded the iodo-derivatives **165** and **166**, which were intended to be used in *Negishi*-type couplings.[92] However, the reactions of **165** and **166** with chlorosilane **158** in presence of $ZnCl_2$ and $Pd(PPh_3)_4$ were not successful,

the RZnCl species not being reactive enough to effect substitution of the Cl at MOTES-Cl. We also tried to attain **153** and **154** by reaction of chlorosilane **158** with a bulky higher-order cuprate, which were reported recently to be readily formed from α-iodo α,β-unsaturated carbonyl compounds.[93] Treatment of **165** and **166** with $(Neopentyl)_2CuLi$, however, led to an oragnometallic species which did not displace the *Cl*-atom at chlorosilane **158**. This might be due to the steric hindrance, which is not only prominent for the cuprate but for the silane too.

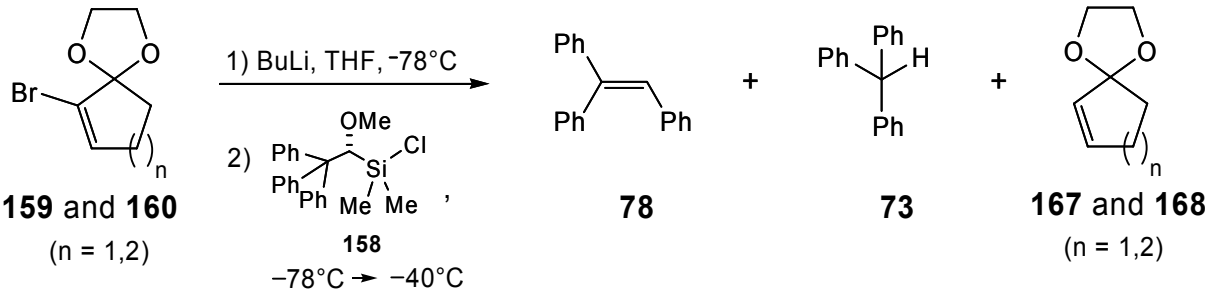


Scheme 45

The focus was therefore shifted towards more reactive, less hindered organometallics, where protection of the carbonyl function, however, was necessary to avoid self-condensation. Thus acetals **167** and **168** were prepared from enones **163**

and **164** by their acid catalized reaction with ethylene glycol in benzene at the water trap. The reaction was high-yielding — in contrast to the transformations performed in toluene, which resulted in lower yields due to the formation of double bond isomers. Brominations of alkenes **167** and **168** proceeded smoothly to afford the α-bromoacetals **159** and **160**[94] which were used as the starting materials for the preparation of the respective metallated derivatives.

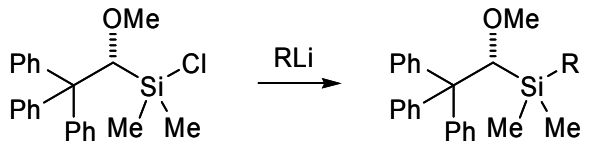
Metallation of the vinyl bromides was in fact successful, their coupling with the silane, however, not. When vinyl bromides **159** and **160** were treated with BuLi and the thus obtained product was added to MOTES-Cl (**158**) at –78 °C in THF, no coupling reactions were observed at all. The starting materials in form of the hydrolyzed products **167** and **168** were only found in the product mixtures. By gradually increasing the temperature to –40 °C, two distinct decomposition products were formed in addition (Scheme 46): triphenylethene (**78**) was found, together with triphenylmethane (**73**), the formation of which is difficult to explain.



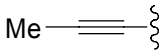
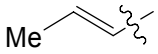
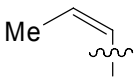
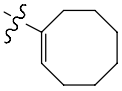
Scheme 46

We finally were interested to learn whether substition at silicon of MOTES-Cl with organometals represents a principal problem. MOTES-Cl was thus reacted with a number of different lithium-derivatives in Et_2O and THF as solvents, and the results of this series of reactions are shown in Table 2.

Table 2. Substitution-reactions at the *Si*-atom of MOTES



158 **157** and **169-173**

Entry	Product	R	Conditions (Et_2O)	Yield (Et_2O)	Conditions (THF)	Yield (THF)
1	**157**		–78 °C to 23 °C	67%	–78 °C to 23 °C	61%
2	**169**	Me	–70 °C	99%	–70 °C	98%
3	**170**	Bu	–78 °C to –35 °C	92%	–78 °C to –35 °C	86%
4	**171**		–110 °C to –70 °C	0%	–110 °C to –63 °C	0%
5	**172**		–110 °C to –73 °C	0%	–110 °C to –65 °C	0%
6	**173**		–110 °C to –65 °C	0%	–110 °C to –68 °C	0%

The results show that both acetylides and alkyllithiums react readily with MOTES-Cl to the respective substitution products **157** and **169**–**170**. The vinyl lithium species — the (*Z*) as well as the sterically less demanding (*E*) isomers — gave rise to decomposition, which occurred, surprisingly, already at temperatures as low as –78 °C to –65 °C (while reactions with alkyl lithiums were still successful, when performed at –78 °C to 23 °C).

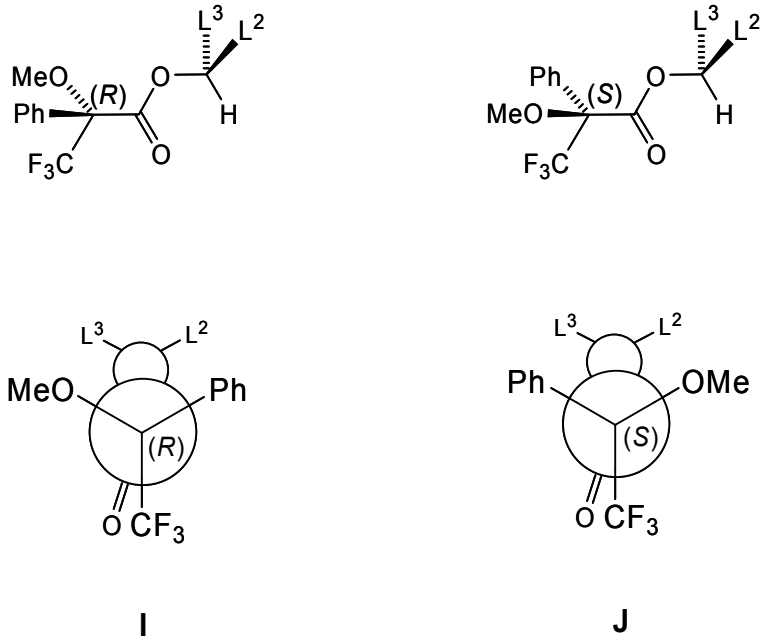
In contrast to the formation of MOTES ethers, which can be performed smoothly, connection of MOTES directly to the carbon-framework proved problematic. The reasons for the observed decompositions are not altogether clear, although it seems evident that an elimination process takes place on the side chain of the MOTES group in presence of *Lewis* acids. Whether these compounds can be prepared by optimizing specific reaction conditions, and whether these species will prove to be stable after isolation, will be subject of future investigations.

3.4. MOTES as a chiral derivatizing agent

As already mentioned in previous sections, we have experienced that diastereomeric MOTES-derivatized products are usually well distinguished in ^{1}H-NMR spectroscopy. Even the addition products of MOTES-protected β-hydroxyaldehydes, where the two stereogenic centers were as far as a six centers apart from each other are distinguishable. There are not many examples in literature, where such a differentiation can be observed for non-rigid open-chain structures.

Since the problem of distinguishing enantiomers/diastereoisomers or, more generally, of establishing absolute and relative configurations of stereogenic centers remains of actual interest, the need for new and complementary chiral derivatizing agent (CDA) is prevailing.

As pointed out in the introductionary part, *Mosher* esterification of secondary alcohols followed by NMR-analysis of the products is one of the most applied methods to distinguish between the enantiomeric forms of the alcohols and to determine their absolute configurations (Figure 14).



I **J**

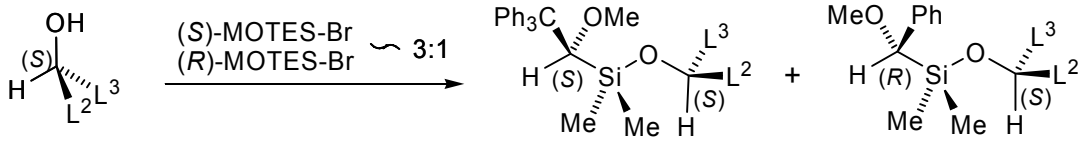
Figure 14

The method relies on the consistent shifts of characteristic peaks in ^{1}H-NMR, depending on the relative configurations of the stereogenic centers of the probe and the chiral derivatizing agent. The method is very reliable; as far as we know, no incorrect absolute configurations that were determined with the *Mosher* method have been reported so far. The explanation of the effect of the *Mosher* group is not fully understood yet, but, as written by *Mosher* in his original paper, "…the observed differences in chemical shifts for the resonances of L^2 and L^3 groups attached to the carbinyl carbon of diastereomeric MTPA esters result from a time weighted average preferential shielding of these groups by the π cloud of the α-phenyl substituents in the acid moiety".

Guided by these concepts, and encouraged by the NMR results obtained previously with the addition products described above, we decided to test whether the MOTES moiety could be used for the NMR differentiation of mixtures of enantiomeric secondary alcohols or α-branched primary amines.

Thus, a number of enantiomerically pure secondary alcohols with known absolute configurations were derivatized with a 3:1 mixture of (*S*)- and (*R*)-MOTES-Br (readily obtained, as previously described, from the correspondent (*S*)- and (*R*)-MOTES-H by bromination) and the silylated products were analyzed by ^{1}H-NMR. The use of (*S*)- and (*R*)-MOTES-Br in a ratio 3:1 was necessary to be able to assign unambiguously the ^{1}H-NMR-peaks to the correspondent isomer. The experiments are summarized in Table 3.

Table 3. MOTES as a chiral derivatizing group.



174–179 **180a–185a** **180b–185b**

Entry	Alcohols	L^2	L^3	Products	$\Delta\delta_a$[a] [ppm]	$\Delta\delta_b$]a] [ppm]
1	**174**	Et	Me	**180a/180b**	0.312	0.324
2	**175**	*i*-Pr	Me	**181a/181b**	0.339	0.332
3	**176**	Ph	Me	**182a/182b**	0.132	0.527
4	**177**	Ph	Et	**183a/183b**	0.144	0.531
5	**178**	Nph	Me	**184a/184b**	0.208	0.541
6	**179**	CO_2Me	Me	**185a/185b**	0.121	0.372

[a] $\Delta\delta_a$ and $\Delta\delta_b$: chemical shift differences in ppm of the diastereotopic Me_2Si.

NMR-data showed that the spectra of the two diastereomeric silylethers are highly distinctive for all MOTES-derivatized alcohols, especially in the region of the diastereotopic Me_2Si where the separation is often very pronounced (see data in Table 3), which allowed for the unambiguous identification and quantification of all isomer pairs. It has to be noticed, however, that the influence of the phenyl groups resulted much stronger on the diastereotopic methyl groups at silicon than on the L^2 and L^3 groups of the alcohols (this effect could not be recorded in the case of MTPA-

esters where, as said, only a carbonyl is present in β-position to the phenyl group). Nevertheless, clear differentiation of signals could be observed for almost every signal of the spectrum (see as an example the spectrum of **184a**/**184b** in Figure 15).

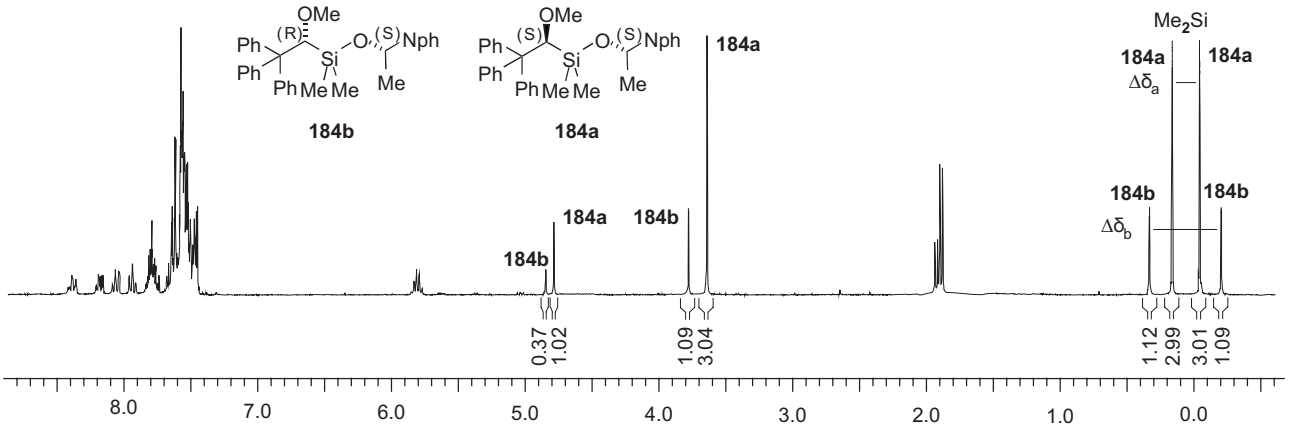
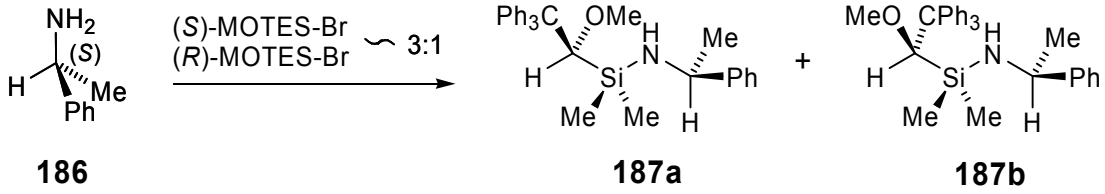


Figure 15. ^{1}H-NMR spec. of the 3:1 mixture of **184a** and **184b** (Entry 5, Table 3).

In addition to these experiments, MOTES was tested as a CDA with a chiral amine too, namely with 1-(*S*)-phenylethylamine (Scheme 47).



186 **187a** **187b**

Scheme 47

Silyl-protected amines **187a** and **187b** were prepared from the free amine and a 3:1 mixture of (*S*)- and (*R*)-MOTES-Br, but these compounds proved unstable when slightly heated or under mild acidic work-up conditions. It was possible, however, to purify the desired products by high vacuum distillation (removing the solvents and the 1-(*S*)-phenylethylamine in excess). The ^{1}H-NMR result of **187a**/**187b** proved consistent with the data obtained with the series of the secondary alcohols (chemical shift differences of the diastereotopic Me_2Si: $\Delta\delta_a$ = 0.084 ppm, $\Delta\delta_b$ = 0.258 ppm).

In addition to the fact that MOTES is well suited as a CDA for the differentiation of enantiomers, the NMR results suggested also a potential application of the MOTES group as a CDA for the direct determination of absolute configurations. Except for the derivatives of the alkyl/alkyl-substituted alcohols, where the diastereomeric silyl ethers are not sufficiently differentiated (Entries 1 and 2, Table 3), the relative shifting of the several signals due to the CDA was consistently related to the relative configurations of the two chiral moieties contained in the molecules: the chemical shift differences of the two MeSi signals of the silylated (*R*,R**)-derivatives ($\Delta\delta_a$) resulted always smaller than those of the two MeSi signals of the (*R*,S**)-derivatives ($\Delta\delta_b$), and in all cases the MeSi signals of the (*R*,R**)-derivatives were enfolded by those of the (*R*,S**)-counterparts.

An explanation of these effects, and whether these patterns prove reliable over a larger range of compounds, is still under study. Compared to the Mosher derivatives, where the informations on the configuration at the carbinyl atom arise from the relative position of the signals of the substituents at this center (L^2 and L^3), in our case a significant differentiation is recorded for the Me_2Si signals of the MOTES group itself. It is not clear yet if the consistency of the pattern of the Me_2Si signals has to be attributed to the Ph_3C group of MOTES, or to the aromatic part of the secondary alcohol, or even to a combination of both elements. The mechanism that could explain these data has necessarily to be investigated in more details; if the same pattern will be observed throughout a larger sample of experiments, however, MOTES could be used not only to quantify diastereomeric reaction mixtures, but also to give important informations on the absolute configurations of the newly formed stereocenters of the final products.

4. Summary – Zusammenfassung

4.1. English version

Silyl moieties have been extensively used in organic chemistry — mainly as protecting or activating moieties but also as auxiliaries for stereoselective synthesis. This treatise presents some applications of a new silicon moiety (MOTES) that is more readily synthesized than previous chiral silicon groups, and not prone to racemization (Figure 16). MOTES was used multipurposely and simultaneously as a protective group, higly efficient chiral auxiliary, and chiral derivatizing agent.

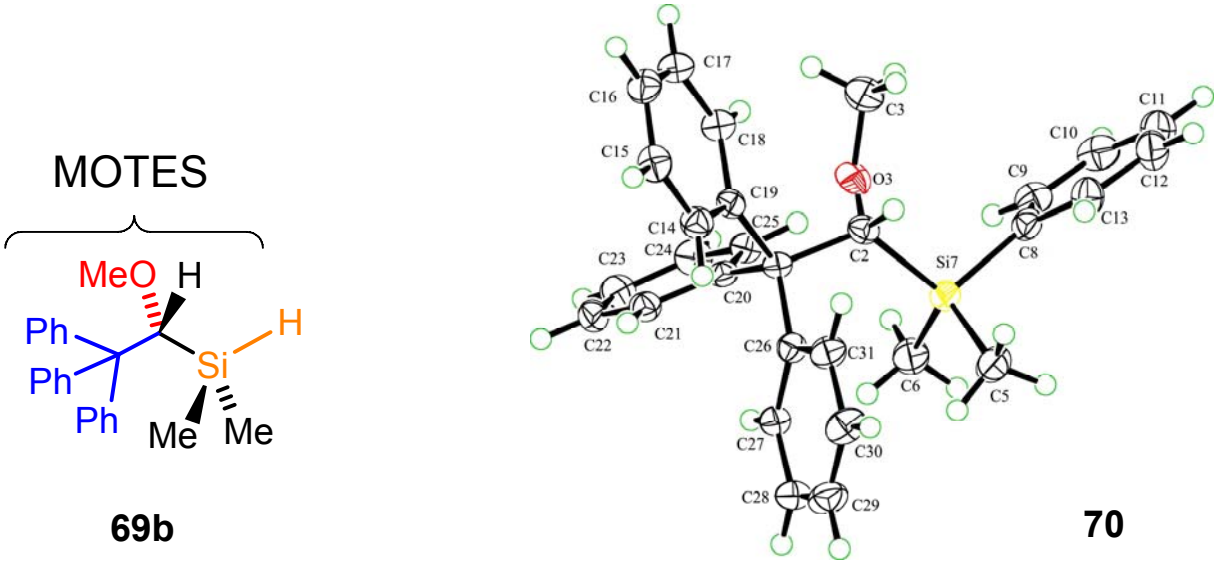
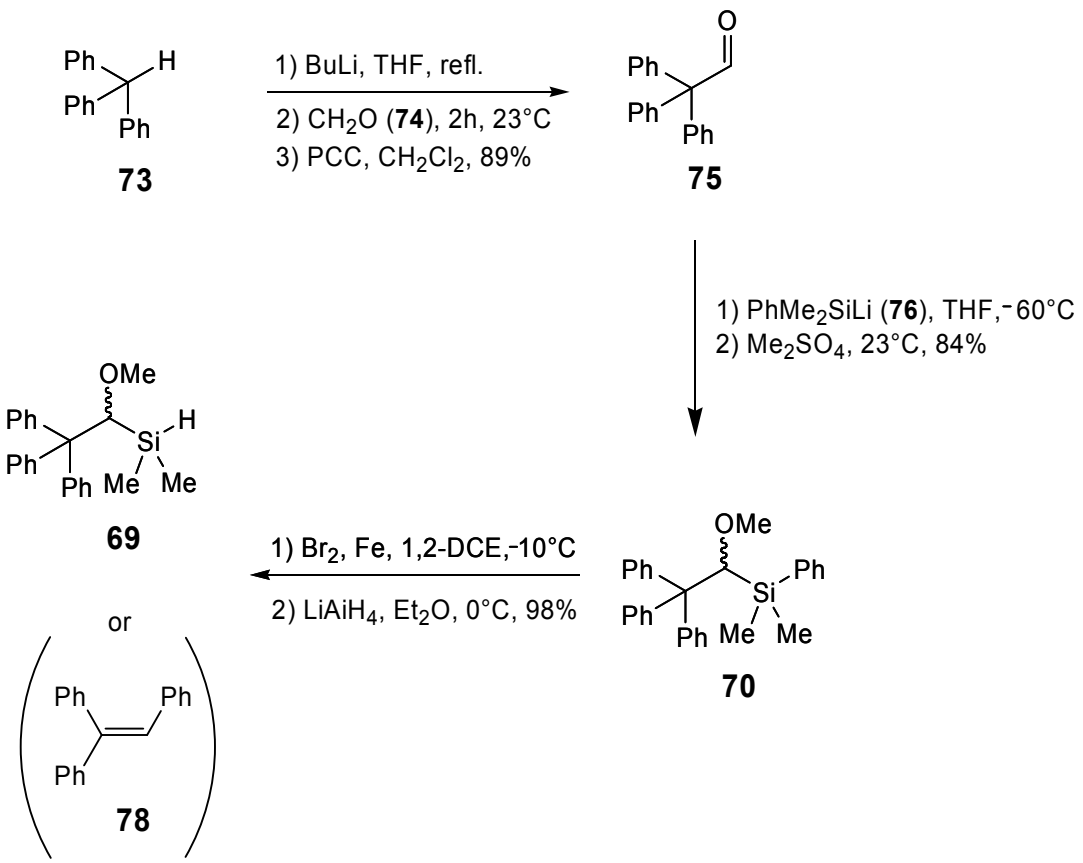


Figure 16. Structure of MOTES-H (**69b**) and X-ray structure of MOTES-Ph (**70**).

Enantiomerically pure silane **69b** [(*R*)-1-methoxy-2,2,2-triphenylethyl)dimethyl silane, MOTES-H] was synthesized from triphenylmethane (**73**) (Scheme 49) according to a procedure that was established by *Trzoss* in his PhD work. In the reproduction of this synthetic scheme, however, some major problems were encountered.

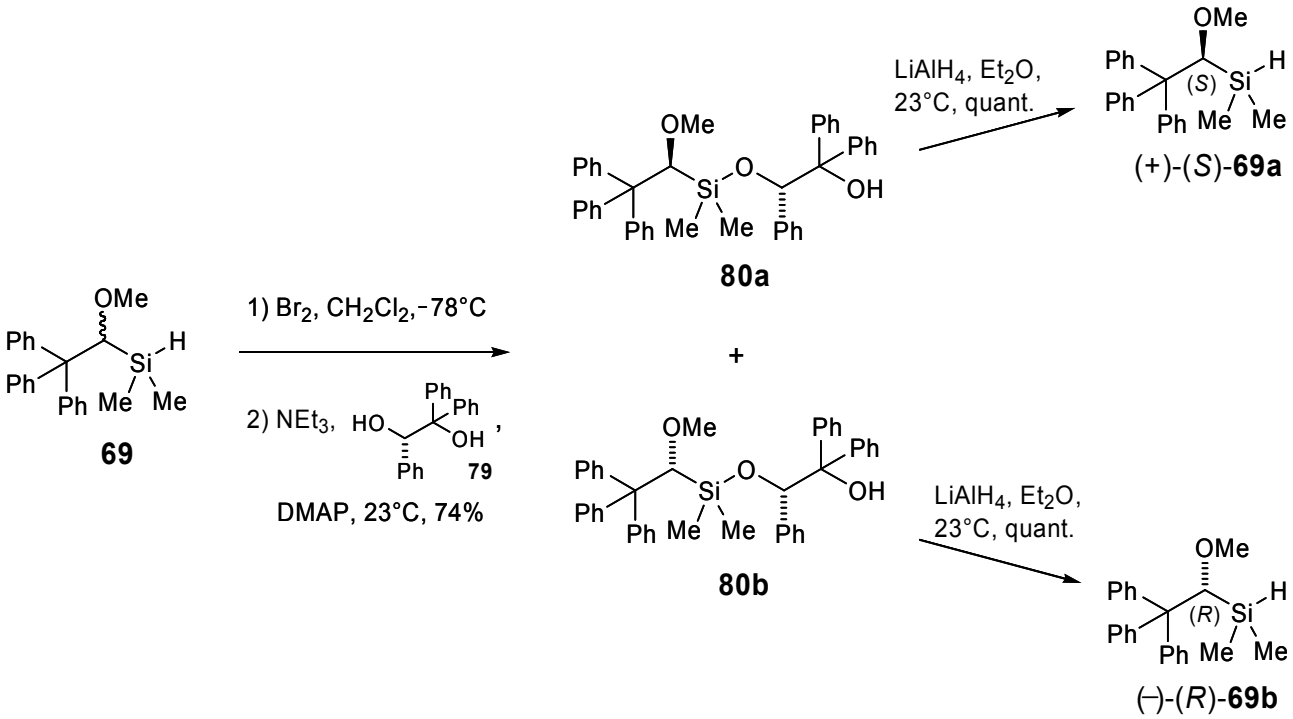


Scheme 49

Upon treatment of **70** with Br_2/Fe and reduction of the intermediate bromosilane with $LiAlH_4$, racemic product **69** did not form reliably but led often to an unexpected decomposition of the silyl moiety to byproduct **78**. This compound was in fact formed quantitatively, as found out, in presence of a larger amount of Fe. This was particularly problematic, since $LiAlH_4$ used in the reduction step contains in variable amounts (up to 10%) Fe as its main impurity. The final optimized procedure requires 5% of Fe-additive in the first step of the reaction, while a commercial solution of $LiAlH_4$ for the reduction in the second step proved more reliable than the $LiAlH_4$ powders.

Resolution of the enantiomers was effected by chromatographic separation of the silylethers obtained with (*S*)-1,1,2-triphenylethane-1,2-diol (**79**), followed by

reduction with $LiAlH_4$, and the absolute configuration of the enantiomers was assigned by X-ray analysis of a crystalline derivative (Scheme 50).

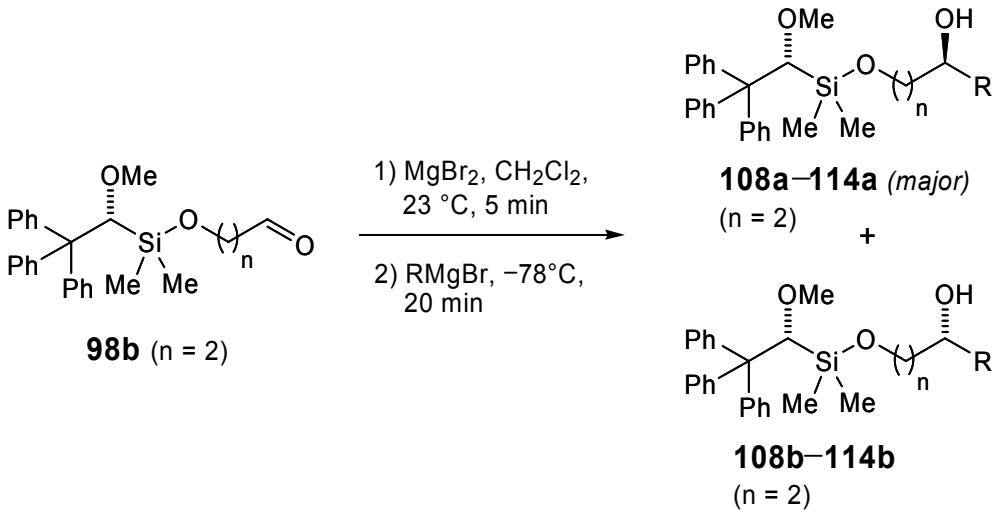


Scheme 50

Motivated by the promising results obtained by *Trzoss* in MOTES-controlled stereoselective additions to α-silyloxyaldehydes, we tried to extend the use of this group to the synthesis of 1,3-diols through nucleophilic additions to MOTES-derived β-hydroxy carbonyl compounds in presence of Mg as a *Lewis* acid.

The results of these transformations are summarized in Table 4. The observed diastereomeric ratios of as high as 16:1 — except for the reaction with the sterically unconstrained ethynyl-*Grignard* reagent — are among the best found for chiral 1,6-inductions so far. The values for the selectivities were established through integration of characteristic peaks in ^{1}H-NMR — typically the singlets deriving from the Me_2Si groups — and confirmed later, on the stage of the MTPA-derivatized alcohols, by analysis of their ^{1}H-NMR and ^{19}F-NMR spectra.

Table 4. Results of MOTES-directed addition reactions.

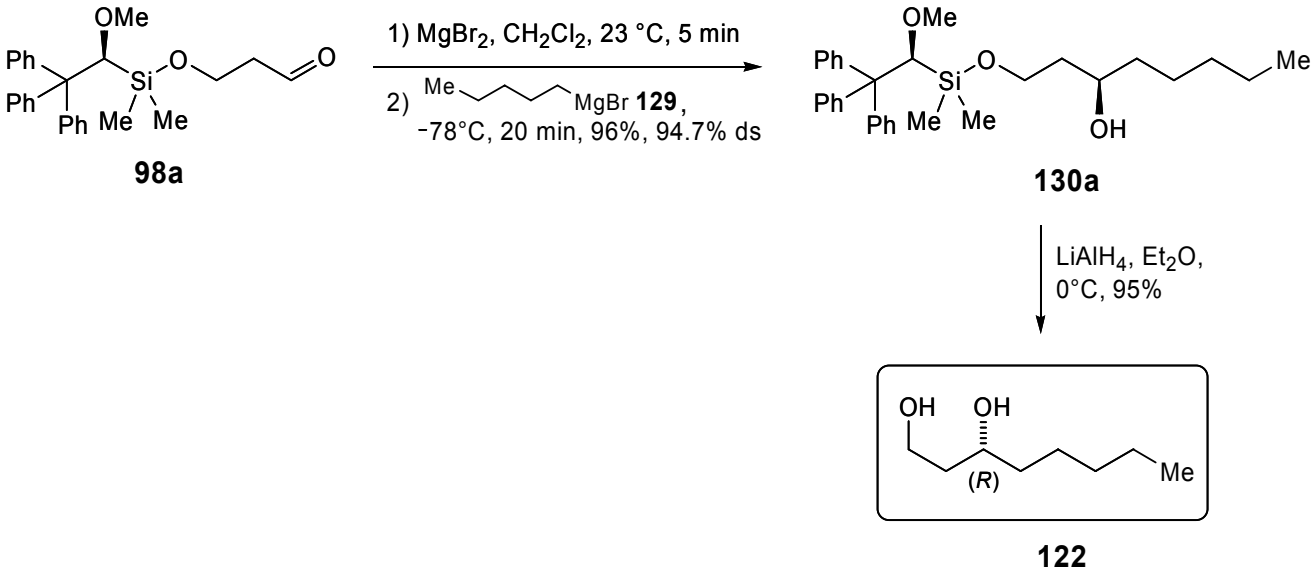


Entry	Educt	Reagent	Product	R	Yield [%][a]	*dr*
1	**98b**	MeMgBr	**108a–108b**	Me	96	14:1
2	**98b**	EtMgBr	**109a–109b**	Et	95	15:1
3	**98b**	*i*-PrMgBr	**110a–110b**	*i*-Pr	96	11:1
4	**98b**	PhMgBr	**111a–111b**	Ph	91	12:1
5	**98b**	AllylMgBr	**112a–112b**	Allyl	98	16:1
6	**98b**	VinylMgBr	**113a–113b**	Vinyl	93	16:1
7	**98b**	EthynylMgBr	**114a–114b**	Ethynyl	97	1:1

[a] Combined yields of the two isomers.

An application of the MOTES group is shown with the enantioselective synthesis of naturally occurring octane-1,3-diol (**122**), identified in 1973 as a natural constituent of apples, and patented one year later for its antimicrobial effects as a food additive (Scheme 51). Enantiopure diol **122** was synthesized in a two-step sequence by addition of pentyl *Grignard* reagent to MOTES-protected β-hydroxyaldehyde **101a** (the desired product **130a** was obtained with 94.7% de). Silylether **130a** could be

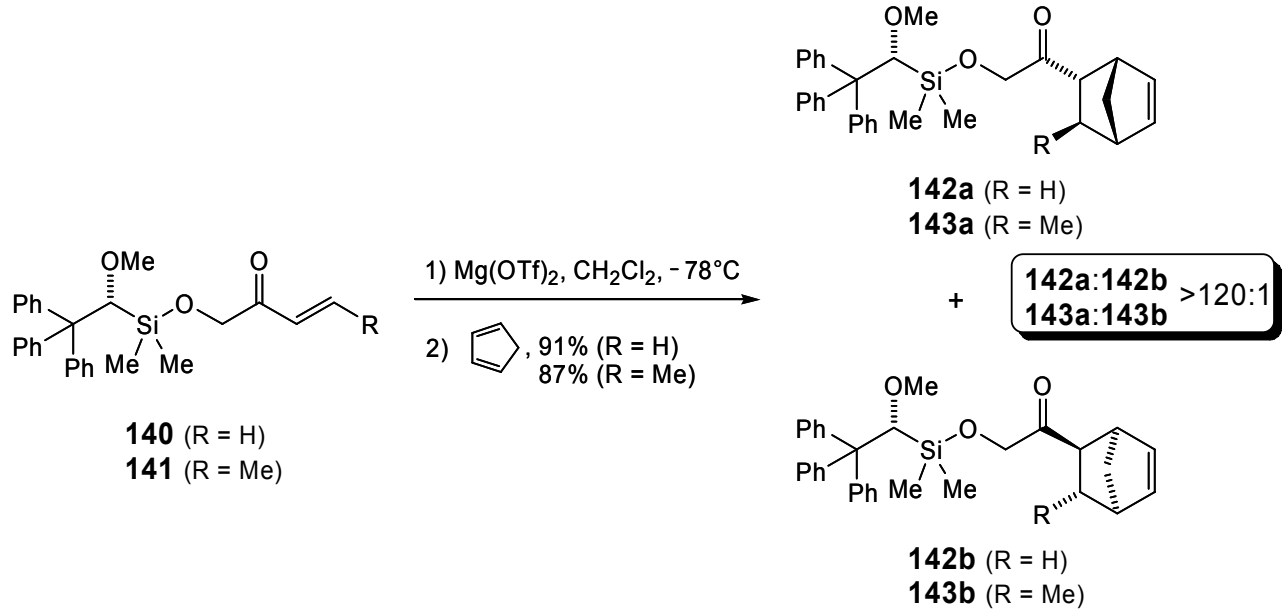
easily separated from the other isomer by preparative TLC, and the subsequent reduction by $LiAlH_4$ afforded MOTES-H (**69a**) and enantiopure diol **122**.



98a **130a** **122**

Scheme 51

This group was futher applied to *Diels–Alder* reactions. After pre-complexation with $Mg(OTf)_2$, MOTES-derivatized α-hydroxy-α',β'-unsaturated carbonyl compounds **140** and **141** were allowed to react with cyclopentadiene at –78 °C and [4+2] cycloadducts were found with dr of up to 120:1 (Scheme 52).



140 (R = H)
141 (R = Me)

142a (R = H)
143a (R = Me)

142b (R = H)
143b (R = Me)

Scheme 52

The stereochemical outcome of the reactions with MOTES-derivatized substrates is consistent with the formation of intermediary tridentate chelate complexes (Figure 17), where the π-facial attack is sterically controlled. It was experienced that the *Lewis*-acid plays a pivotal role with regard to the extent of the selectivities — without pre-complexation of the substrates, distinctively lower selectivities were observed for all transformations.

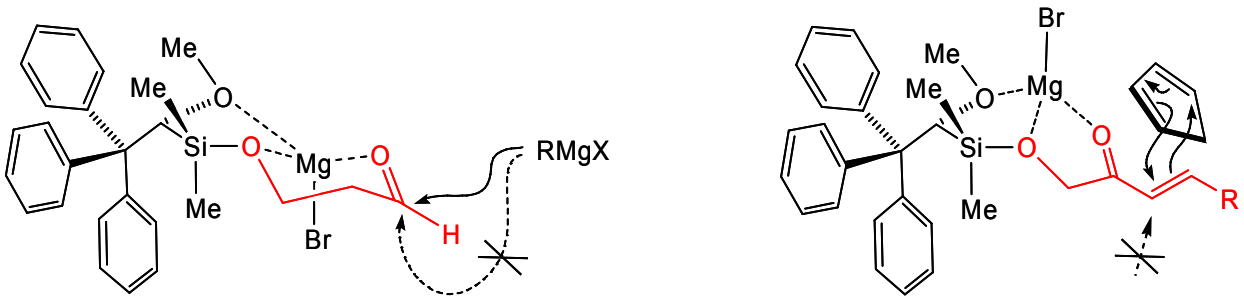
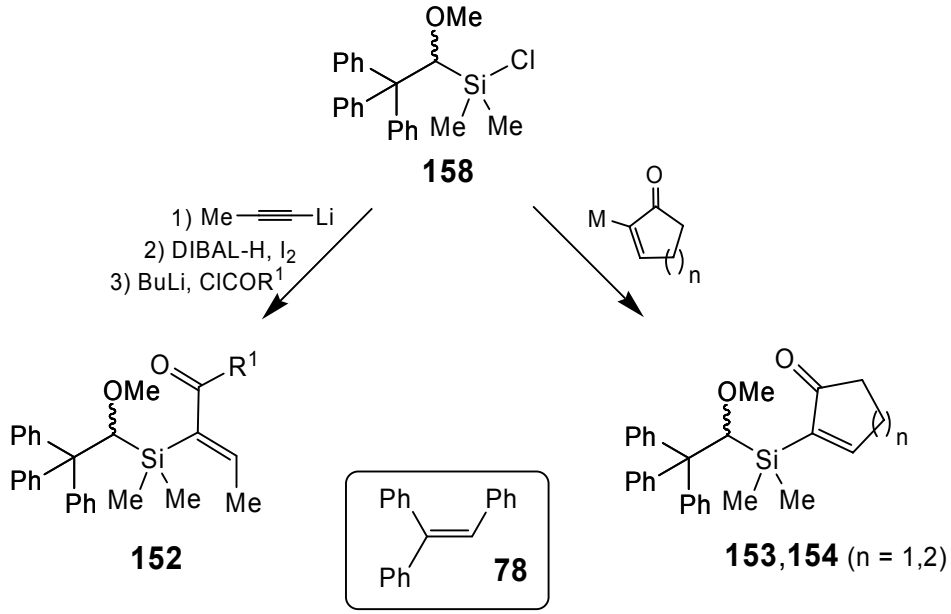


Figure 17. Proposed transition structures for the MOTES-directed reactions.

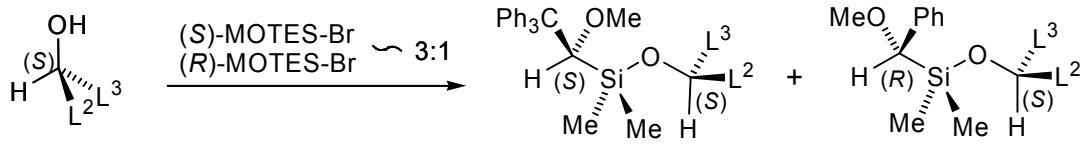
We also tried to explore the effect of the MOTES group upon diastereoselective reactions when the auxiliary was linked directly to the carbon framework of the substrate. Specifically, we intended to open access to target compounds of type **152** and **163**–**164** (Scheme 53), envisioned as suitable starting materials for chelate-controlled cuprate additions. Two different synthetic strategies were tested to obtain the target structures, but both procedures proved unsuccessful due to the formation in the last steps of the already encountered decomposition product triphenyl ethane (**78**).



Scheme 53

The ease, by which we were able to distinguish the diastereomeric products of our stereoselective MOTES-controlled transformations by NMR, suggested that the MOTES group could also be applied as a silicon-based chiral derivatizing agent (CDA). Thus, a number of diastereomeric pairs of silyated secondary alcohols were prepared and studied by ^{1}H-NMR (Table 5).

Table 5. MOTES as a chiral derivatizing group.



174–179 **180a–185a** **180b–185b**

Entry	Alcohols	L^2	L^3	Products	$\Delta\delta_a$ [a] [ppm]	$\Delta\delta_b$ [a] [ppm]
1	**174**	Et	Me	**180a**/**180b**	0.312	0.324
2	**175**	*i*-Pr	Me	**181a**/**181b**	0.339	0.332
3	**176**	Ph	Me	**182a**/**182b**	0.132	0.527
4	**177**	Ph	Et	**183a**/**183b**	0.144	0.531
5	**178**	Nph	Me	**184a**/**184b**	0.208	0.541
6	**179**	CO_2Me	Me	**185a**/**185b**	0.121	0.372

[a] $\Delta\delta_a$ and $\Delta\delta_b$: chemical shift differences in ppm of the diastereotopic Me_2Si.

Particularly the derivatives of the α-aryl/alkyl- and alkoxycarbonyl/alkyl-substituted alcohols, compounds **182a**–**185a** and **182b**–**185b**, showed highly distinctive spectra, which allows for unambiguous identification and quantification of the compounds (Table 5).

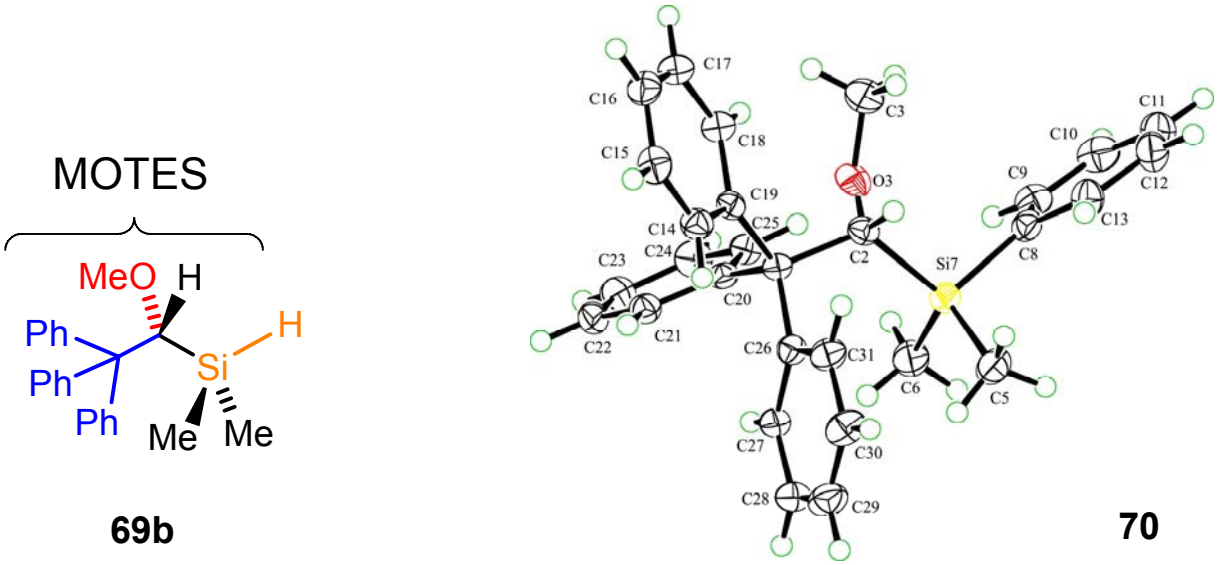
The NMR results suggested also a potential application of the MOTES group as a CDA for the direct determination of absolute configurations. Except for the derivatives of the alkyl/alkyl-substituted alcohols, the relative shifting of several signals due to the CDA was distinctive enough and consistently related to the relative configurations of the two chiral moieties contained in the molecules. Whether this pattern proves reliable over a larger range of compounds is presently under investigation.

In conclusion, the MOTES group was shown to act efficiently as a multipurpose tool in synthetic chemistry. This moiety can be easily attached to a free hydroxyl function

for its protection, and the formed silylethers are particularly stable to several reaction conditions and to SiO_2-chromatography. Its removal from the substrate is still easily performed by reduction with $LiAlH_4$ or by treatment with fluoride, and the MOTES can be fully recovered at any stage. Simoultaneously, in presence of *Lewis* acids, MOTES acts as a powerful stereo-directing group for several reactions where chelate-transition-structures are possible. Finally, most of the diastereomeric mixtures obtained by MOTES-directed transformations could be quantified by analysis of their ^{1}H-NMR spectra. In addition, the spectra of diastereomeric MOTES-ethers of secondary alcohols proved not only distinctive enough, but also consistently related to the relative configurations of the two stereogenic centers: for this reason, the MOTES-group allows not only a secure distinction of diastereomeric products, but also — eventually — the determination of absolute configurations. We believe that this group can be successfully applied in an even broader context to any substrate that is able to chelate during the course of a specific transformation.

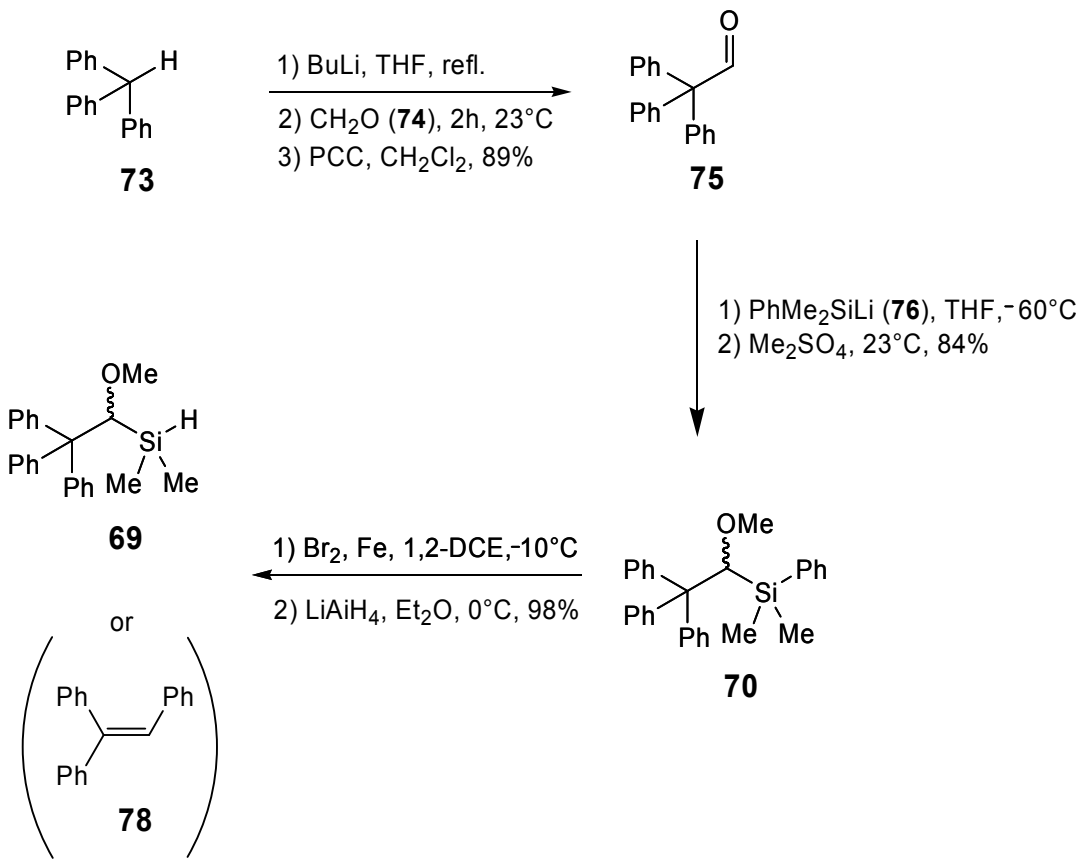
4.2. Deutsche Version

Silylgruppen werden in der Organischen Chemie ausgiebig verwendet — hauptsächlich als Schutz- oder als Aktivierungs-Gruppe, aber auch als Auxiliar für stereoselektive Synthesen (Figur 16). In dieser Arbeit zeigen wir einige Anwendungen einer neuen chiralen Silicium-Gruppe, MOTES, die im Vergleich zu früher verwendeten chiralen Silicium-Gruppen einfacher zu synthetisieren ist und nicht racemisieren kann. Wir haben die MOTES-Gruppe multifunktional eingesetzt: Sie wirkte gleichzeitig als Schutzgruppe, und sehr effizientes chirales Auxiliar, und als differenzierende Gruppe bei der Analyse von Stereoisomeren.



Figur 16. Struktur von MOTES-H (**69b**) und X-ray Analyse von MOTES-Ph (**70**)

Enantiomerenreines Silan **69b** wurde nach einer Vorschrift, die *Trzoss* im Rahmen seiner Dissertation erarbeitet hatte, aus Triphenylmethan (**73**) synthetisiert (Schema 49). Beim Versuch, die Angaben von *Trzoss* zu reproduzieren, sind jedoch unerwartete Schwierigkeiten aufgetaucht.

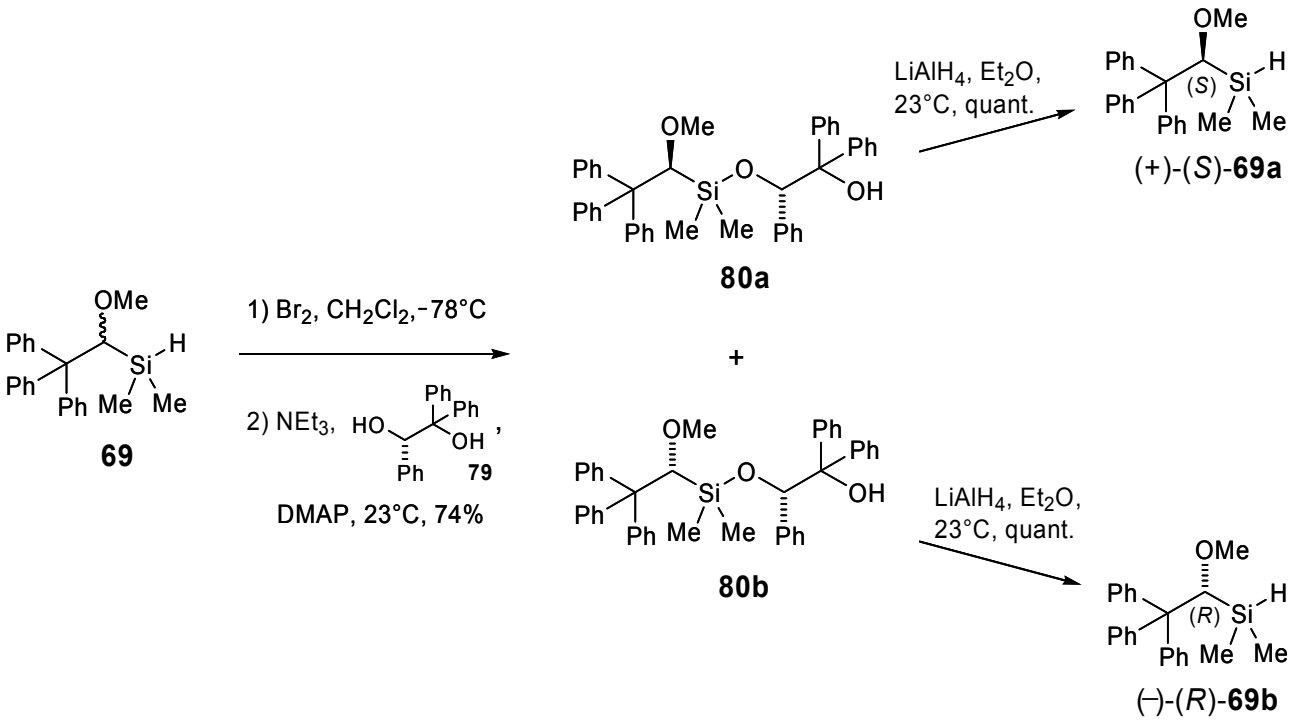


Schema 49

Behandlung von **70** mit Br_2/Fe, gefolgt von Reduktion des intermediären Bromosilans mit $LiAlH_4$, ergab nicht zuverlässig das erwartete racemisches Hydrosilan **69**, sondern führte oft zu beträchtlichen Mengen Triphenylethen (**78**), welches durch Zersetzung der Silicium-Einheit gebildet wurde. Das Produkt **78** wird tatsächlich in quantitativer Ausbeute gewonnen, wenn mit einer grösseren Menge an Fe im ersten Schritt der Transformation gearbeitet wird. Diese Beobachtung war deshalb von besonderer Bedeutung, da kommerzielles $LiAlH_4$ bis zu 10% mit Fe verunreinigt sein kann, was die Kontrolle über die genaue Menge an im Gemisch (beim zweiten Schritt) letztlich vorliegenden Fe verunmöglicht. In einer optimierten Prozedur wird nun 5% Fe-additiv im ersten Schritt der Reaktion eingesetzt sowie, für die Reduktion im zweiten Schritt, eine kommerziell erhältlich Lösung von $LiAlH_4$ in

THF, welche verlässlichere Resultate lieferte als das früher verwendete $LiAlH_4$-Pulver.

Das auf diese Weise erhaltene racemische Hydrosilan **69** wurde nach bewährter Vorschrift durch Racematspaltung in die Enantiomeren aufgetrennt. Die Racematspaltung erfolgte dabei durch chromatographische Trennung der beiden durch Silylierung von (*S*)-1,1,2-Triphenylethan-1,2-diol (**79**) erhaltenen Silylether **80a** und **80b**, welche anschliessend durch Reduktion mit $LiAlH_4$ in die Hydrosilane (+)-(*S*)-**69a** und (–)-(*R*)-**69b** zurück geführt wurden (Schema 50). Die absoluten Konfigurationen der Silane wurde durch Einkristallröntgenstrukturanalyse mit einem kristallinen Derivat bestimmt.

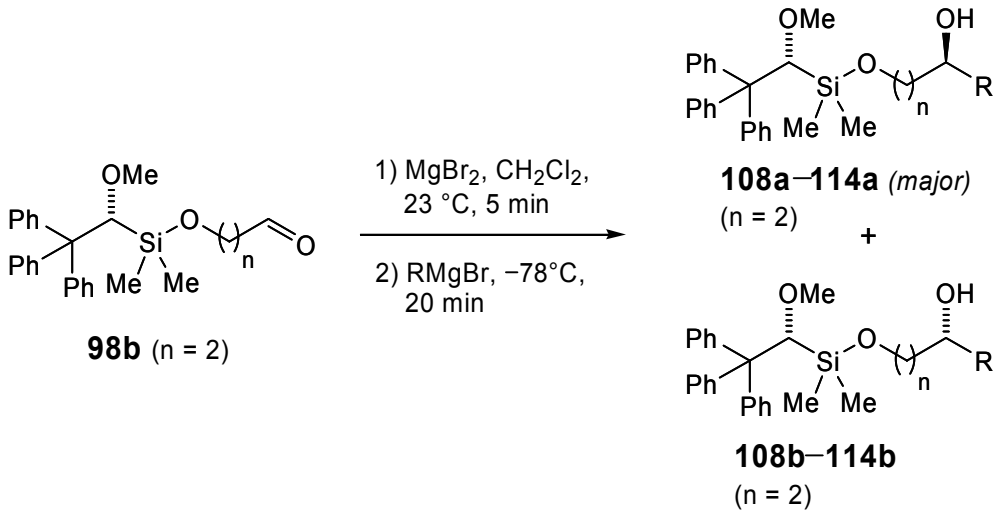


Schema 50

Motiviert durch die vielversprechendenden Resultate von *Trzoss* in seinen MOTES-kontrollierten stereoselktiven Additionen an α-Silyloxyaldehyde, versuchten wir die Anwendung von MOTES mit *Lewis* Säure-katalysierten nucleophilen Additionen an MOTES-derivatisierte β-Hydroxy-Carbonylverbindungen zur Synthese von 1,3-

Diolen zu erweitern. Die Reaultate dieser Untersuchungen sind in Tabelle 4 zusammengefasst. Die beobachteten Diastereomerenverhältnisse betrugen bis zu 16:1 — ausser für die Reaktion mit dem linearen Ethinyl-MgBr Reagens — und gehören damit zu den besten Selektivitäten, die bisher für chiralie 1,6-Induktionen gefunden wurden. Diese Diastereomerenverhältnisse wurden durch Integration charachteristischer Signale im ^{1}H-NMR-Spektrum ermittelt — typischerweise der Singuletts der Me_2Si — und später, auf der Stufe der MTPA-derivatisierten Alkohole, durch Analyse deren ^{1}H-NMR- and ^{19}F-NMR-Spektren bestätigt.

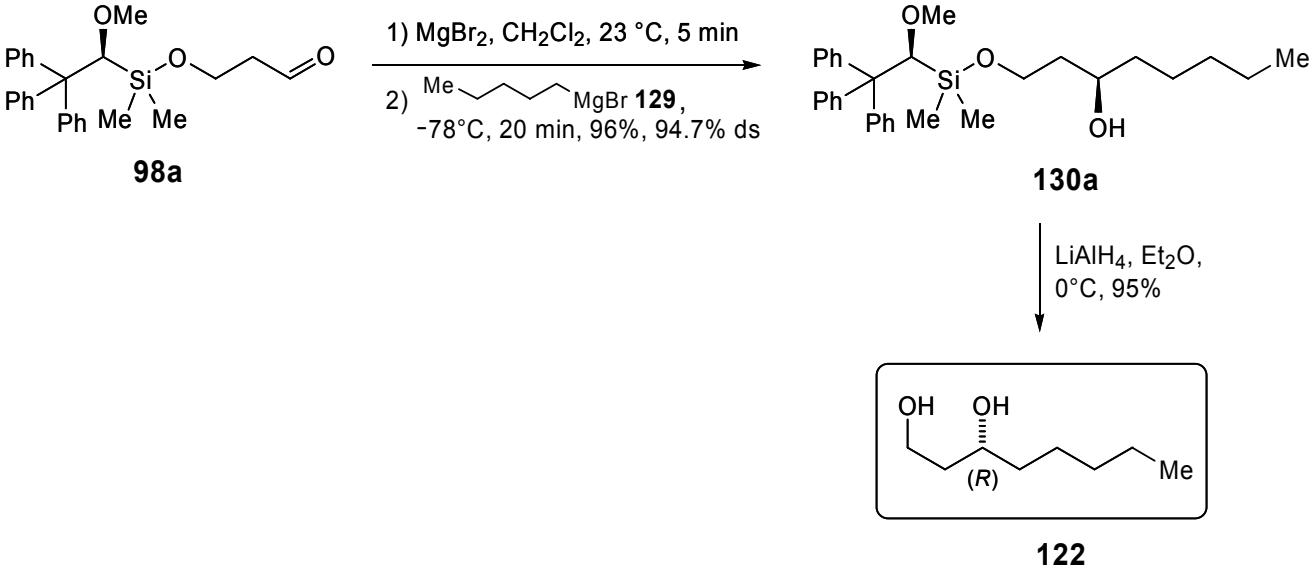
Table 4. Resultate der MOTES-dirigierten Additions-Reaktionen.



Entry	Educt	Reagent	Product	R	Yield [%][a]	*dr*
1	**98b**	MeMgBr	**108a–108b**	Me	96	14:1
2	**98b**	EtMgBr	**109a–109b**	Et	95	15:1
3	**98b**	*i*-PrMgBr	**110a–110b**	*i*-Pr	96	11:1
4	**98b**	PhMgBr	**111a–111b**	Ph	91	12:1
5	**98b**	AllylMgBr	**112a–112b**	Allyl	98	16:1
6	**98b**	VinylMgBr	**113a–113b**	Vinyl	93	16:1
7	**98b**	EthynylMgBr	**114a–114b**	Ethynyl	97	1:1

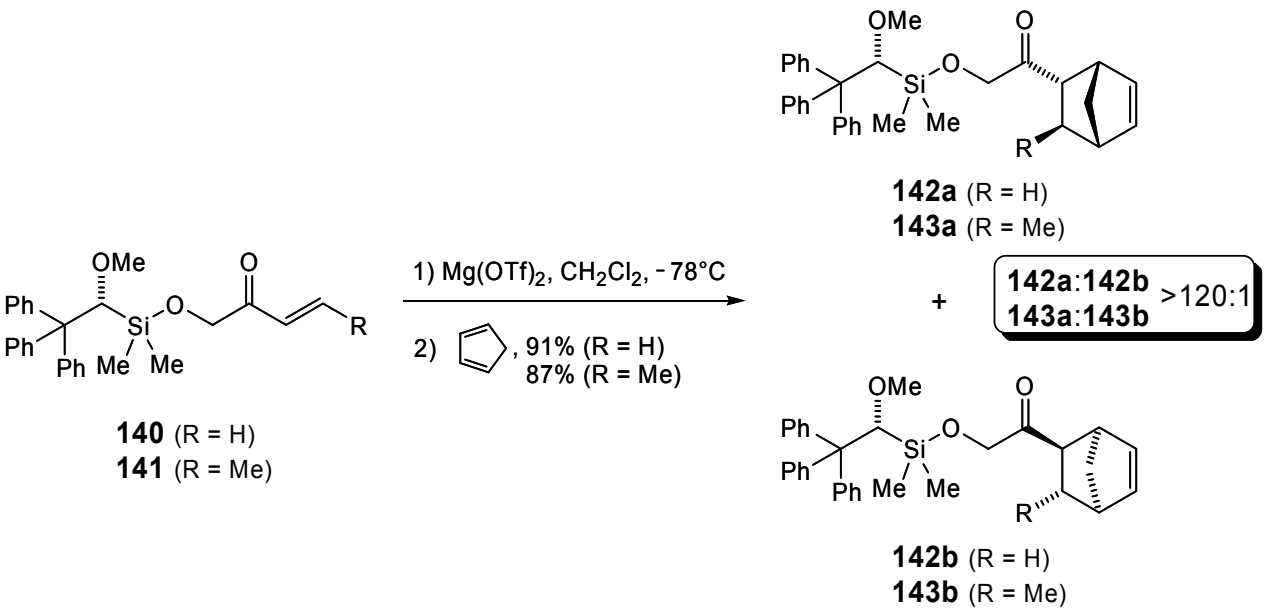
[a] Ausbeute an vereinigten Produkten.

Eine Anwendung der MOTES-Gruppe ist mit der enantioselctiven Synthese von natürlich vorkommendem (*R*)-Octan-1,3-diol (**122**) gezeigt (Schema 51). Dieses Diol wurde 1973 als ein Bestandteil von Äpfeln identifiziert und ein Jahr später für seine antimikrobiologischen Eigenschaften als Nahrungsmittelergänzung patentiert. Die Verbindung wurde durch Addition von Pentyl-*Grignard*-Reagenz an den MOTES-geschützten β-Hydroxyaldehyd **98a** in einer Zweistufen-Sequenz in insgesamt 91% Ausbeute und mit 88% ee synthetisiert.



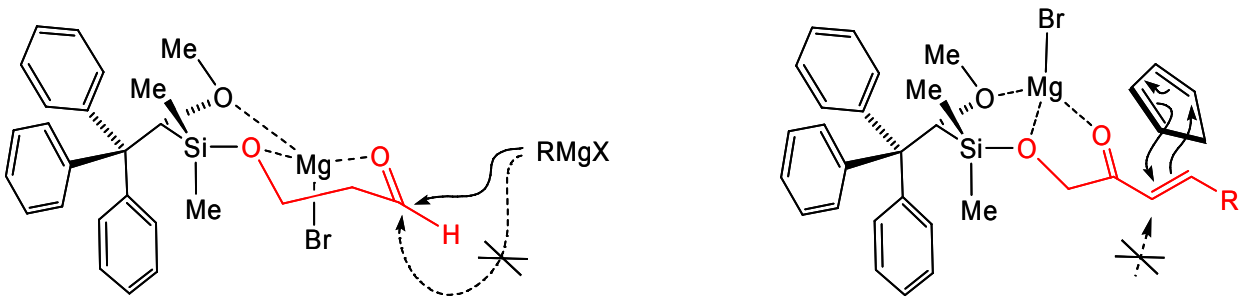
Scheme 51

Die MOTES-Gruppe wurde im Weiteren auch für der *Diels–Alder*-Reaktion angewandt. Nach Vorkomplexierung der MOTES-derivatisierten α-Hydroxy-α',β'-ungesättigten Carbonylverbindungen **140** and **141** mit *Lewis*-Säure und anschliessender Umsetzung bei –78 °C mit Cyclopentadien bildeten sich die erwarteten [2+4]-Cycloaddukte mit guten Ausbeuten und hohen Stereoselektivitäten (dr bis 120:1) (Schema 52).



Schema 52

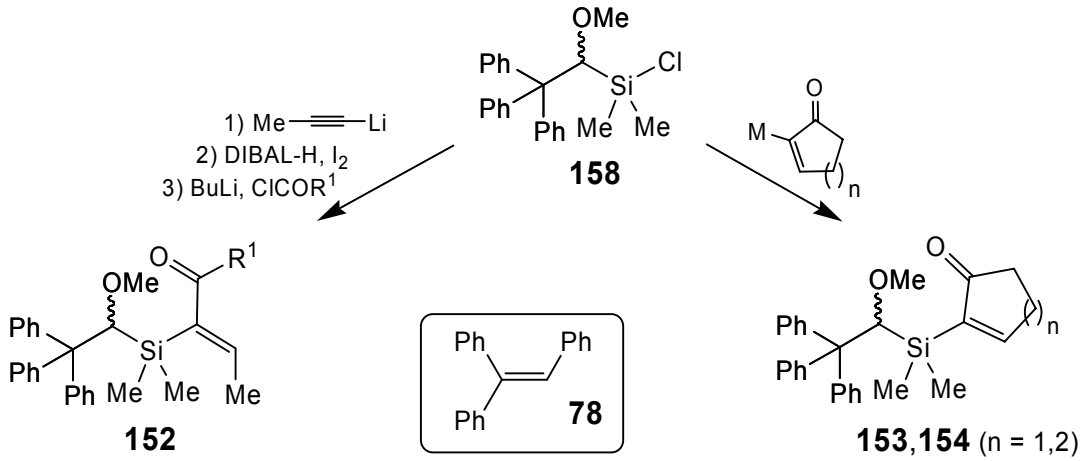
Der Stereochemische Verlauf der Reaktionen mit den MOTES-derivatisierten Substraten kann mit der Bildung intermediärer tridentater Chelat-Komplexe erklärt werden (Figur 17), bei welchen die π-Seiten-Differenzierungen sterisch bedingt sind. Es wurde festgestellt, dass die Chelat-ermöglichenden *Lewis*-Säure-Additive eine wichtige Rolle für die Höhe der Selektivitäten spielen — ohne Zugabe von *Lewis*-Säuren wurden durchwegs tiefere Selektivitäten (oder überhaupt keine mehr) gefunden.



Figur 17

Wir haben auch versucht, den Effekt der MOTES-Gruppe auf diastereoselektive Transformationen an Molekülen zu untersuchen, bei welchen die Silicium-Gruppe

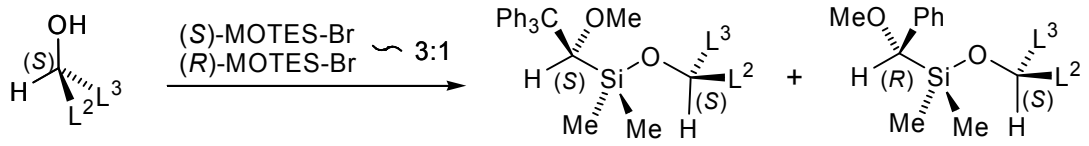
direkt mit dem Kohlenstoffgerüst verknüpft ist. Konkret wollten wir Verbindungen des Typs **152** und **153**/**154** untersuchen, welche aber vorerst selbst zugänglich gemacht werden mussten (Schema 53). Wir haben versucht, diese Verbindungen auf zwei Wegen herzustellen, scheiterten jedoch daran, dass jeweils im letzten Schritt der Reaktionssequenzen Zersetzung der Silicium-Gruppierung eintrat — unter Bildung des uns bereits bekannten Triphenylethens (**78**).



Scheme 53

Da es jeweils einfach war, die Produkte unserer MOTES-kontrollierten stereoselektiven Trasformationen mittels ^{1}H-NMR zu differenziern, wollten wir die MOTES-Gruppe auch als ein Silicium-basierendes chirales Derivatisierungs-Reagenz testen. Zu diesem Zweck wurde eine Reihe diastereomerer Paare silylierter sekundärer Alkohole hergestellt und mittels ^{1}H-NMR untersucht (Tabelle 5).

Table 5. Die MOTES-Gruppe als chirales Derivatisierungs-Reagenz.



174–**179** **180a**–**185a** **180b**–**185b**

Entry	Alcohols	L^2	L^3	Products	$\Delta\delta_a$[a] [ppm]	$\Delta\delta_b$[a] [ppm]
1	**174**	Et	Me	**180a**/**180b**	0.312	0.324
2	**175**	*i*-Pr	Me	**181a**/**181b**	0.339	0.332
3	**176**	Ph	Me	**182a**/**182b**	0.132	0.527
4	**177**	Ph	Et	**183a**/**183b**	0.144	0.531
5	**178**	Nph	Me	**184a**/**184b**	0.208	0.541
6	**179**	CO_2Me	Me	**185a**/**185b**	0.121	0.372

[a] $\Delta\delta_a$ und $\Delta\delta_b$: Unterchied in ppm der diastereotopischen Me_2Si.

Speziell die Derivate der α-Aryl/Alkyl- und α-Alkoxycarbonyl/Alkyl-substituierten Alkohole, (Verbindungen **182a**–**185a** und **182b**–**185b**) zeigten deutlich unterschiedliche Spektren, welche eine eindeutige Identifikation und Quantifizierung der Verbindungen ermöglichten. (Tabelle 5).

Die NMR-Daten deuten an, dass die MOTES-Gruppe möglicherweise eine Anwendung als CDA für die direkte Bestimmung von absoluten Konfigurationen bieten könnte. Ausser für die Derivate der α-Alkyl/Alkyl-substituierten Alkohole sind die relativen Verschiebungen verschiedener Signale aufgrund des CDA genügend differenziert und einheitlich korrelierbar mit den relativen Konfigurationen der zwei chiralen Einheiten der Moleküle. Ob sich dieses Muster über eine breitere Auswahl an Verbindungen als zuverlässig erweist wird zurzeit noch untersucht.

Zusammenfassend konnte gezeigt werden, dass die MOTES-Gruppe sowohl eine effiziente Schutz- und stereodirigierende Gruppe ist, wie auch ein Potential als chiral-differenzierende Gruppe in einem CDA zur Unterscheidung enantiomerer Alkohole und zur Bestimmung derer absoluten Konfigurationen besitzt. Bei MOTES-dirigierten stereoselektiven Transformationen von MOTES-derivatisierten α- und β-Hydroxyaldehyden und -enonen wurden Diastereoselektivitäten von bis zu 98.8 % gefunden, welche durch 1,6-chirale Induktion zustande kamen. Wir sind der Überzeugung, dass die MOTES-Gruppe noch bei weiteren Substraten und Reaktionen angewendet werden kann; in Kombination mit jeglichen Substanzen, die in der derivatisierten Form Chelate bilden können, welche ihrerseits die π-Seiten-Differenzierung für eine Reaktion an einer prostereogenen Einheit des Moleküls erhöht.

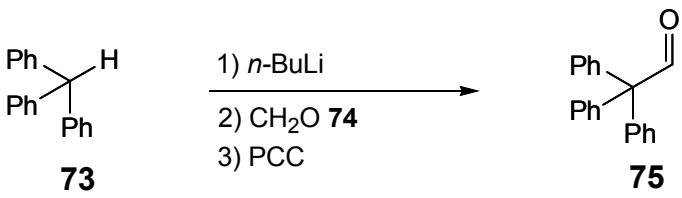
5. Experimental part

5.1. General remarks

Unless otherwise stated, manipulations were carried out under Ar in oven-dried glass equipment. For reactions, Et_2O and THF were freshly distilled from Na with benzophenone ketyl as indicator. Solns. for workup procedures were prepared in deionised H_2O. Solns. of $LiAlH_4$ in Et_2O (1.0 M) commercially available (Sigma-Aldrich). Chromatography: Merck silica gel 60 (40–63 μm). IR spectra: neat liquid films between NaCl plates; *Perkin-Elmer* IR "Spectrum One" and *Perkin-Elmer* 781; in cm^{-1}. ^{1}H-NMR spectra in $CDCl_3$; *Bruker AC-300* (300 MHz); δ in ppm rel. to $CHCl_3$ (δ 7.26), *J* in Hz. ^{13}C-NMR spectra in $CDCl_3$; *Bruker AC-300* (75.5 MHz); δ in ppm rel. to $CDCl_3$ (δ 77.0); ^{19}F-NMR spectra in $CDCl_3$ *Bruker AC-300* (282.4 MHz); multiplicities from DEPT-135 and DEPT-90 experiments. ESI mass spectra were performed on a *Bruker ESQUIRE-LC* quadrupole ion trap instrument (*Bruker Daltonik GmbH,* Bremen, Germany), equipped with a combined Hewlett-Packard Atmospheric Pressure Ion (API) source (*Hewlett-Packard Co.*, Palo Alto, CA, USA). EI and CI mass spectra were performed on a sector field mass analyzer (*Finnigan MAT95*, San Jose, CA; USA); the ionization energy was 70 eV for EI and 150 eV for CI with NH_3 as reactant gas. Quasi-molecular ions and characteristic fragments in *m/z* (rel. %).

5.2. Synthesis of MOTES-H

Triphenylacetaldehyde (75)



73 **75**

A soln. of BuLi in Et_2O (1.6 M, 50.8 mL) was added at 23 °C to a soln. of triphenylmethane (**73**) (20.0 g, 80.80

mmol) in THF (160.0 mL) and stirred vigorously. The mixture was heated to reflux and stirring was prolonged for 1.5 h. The red soln. was cooled to 15 °C and formaldehyde (7.4 g, 204.8 mmol) was added. After 3 h, the solvent was removed under reduced pressure, CH_2Cl_2 (140.0 mL) was added, and the soln. was cooled to 0 °C. PCC (21.6 g, 100.40 mmol) was added, the temperature was increased to 23 °C, and the mixture was stirred for 3 h. Filtration on a double layer of silica-gel and celite, and evaporation of the solvent under reduced pressure afforded triphenylacetaldehyde (**75**) (19.53 g, 71.20 mmol, 89%). Analytical data in agreement with the one reported in literature.[95]

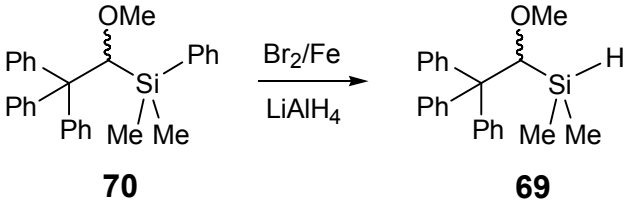
(±)-(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)phenylsilane (70)

75 **70**

Li (1.55 g, 252.43 mmol) was added to a soln. of $PhMe_2SiCl$ (14.2 mL, 85.51 mmol) in THF (100 mL) at 0 °C and the mixture was stirred for 8 h. [60] After this time, the soln. was transferred with a *cannula* into a second flask, containing a soln. of triphenylacetaldehyde (**75**, 10.50 g, 50.51 mmol) in THF (200.0 mL) at –60 °C, and the mixture was stirred for 30 min at –30 °C. Me_2SO_4 (20.5 mL, 216.2 mmol) was then added and the stirring prolonged for 6 h at 23 °C. The reaction was quenched with a sat. aq. soln. of NH_4Cl (300 mL), the layers were separated, and the aq. phase was extracted with Et_2O (2 x 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude mixture was purified by recrystallization (hexane/EtOAc 50:1) to afford **70** as colorless crystals (2.20 g, 5.21 mmol, 84%). M.p.: 59–61 °C (hexane). IR: 3050*s*, 2960*s*, 2920*s*, 2890*s*, 2810*s*, 1490*s*, 1445*s*, 1435*s*, 1245*s*, 1110*s*, 1090*s*, 1080*s*, 840*s*, 815*s*. ^{1}H-NMR: 7.56–7.52, 7.37–7.14 (2*m*, 20 arom. H); 4.56 (*s*, SiCH); 3.10 (*s*, MeO); –0.10, –0.11 (2*s*, Me_2Si). ^{13}C-NMR: 145.9 (*s*, 3 arom. C); 140.6 (*s*, arom. C); 134.0, (*d*, 3 arom. C); 130.3 (*d*, 6 arom. C); 128.7, 127.7 (2*d*, 2 x 2 arom. C); 127.3

(*d*, 6 arom. C); 126.0 (*d*, arom. C); 83.5 (*d*, SiCH); 61.7 (*s*, Ph_3C); 61.5 (*q*, MeO); –0.3, –3.8 (2*q*, Me_2Si). CI-MS: 440 (16, $[M+NH_4]^+$); 243 (100, $[Ph_3C]^+$).

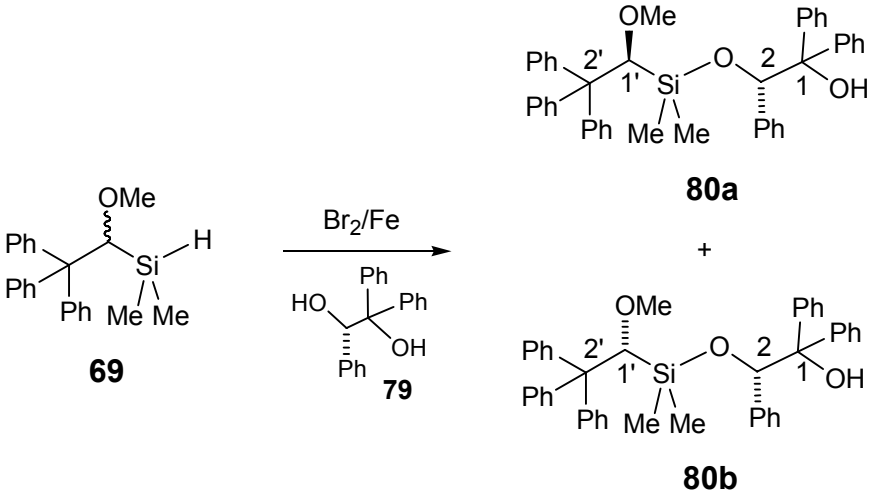
(±)-(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silane (69)



70 **69**

Fe (21.1 mg, 0.47 mmol) was added to a soln. of **70** (4.22 g, 10.00 mmol) in 1,2-dichloroethane (150.0 mL). The mixtures was cooled to –10 °C and Br_2 (0.67 mL, 10.30 mmol) was added dropwise. After complete consumption of the starting material (monitored by TLC, ca. 1.5 h), a soln. of $LiAlH_4$ (1.0 M, 10.5 mL, 10.50 mmol) in Et_2O was added at 0 °C, and it was stirred for 3 h at 23 °C. The excess of $LiAlH_4$ was neutralized with an aq. soln. of H_2SO_4 (10%), and the layers were separated. The aq. phase was extracted with Et_2O (2 x 100 mL) and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2; hexane/EtOAc 50:1) afforded **69** as a colorless viscous oil (3.29 g, 9.8 mmol, 98%). IR: 3050*s*, 2960*s*, 2920*s*, 2875*s*, 2868*s*, 2140*s*, 1490*s*, 1445*s*, 1250*s*, 1095*s*, 880*s*. ^{1}H-NMR: 7.28–7.13 (*m*, 15 arom. H); 4.41 (*d*, $J = 1.0$, SiCH); 3.76 (*dsept*, $J = 1.0$, 3.8, SiH); 3.35 (*s*, MeO); 0.13, –0.44 (2*d*, $J = 3.8$, Me_2Si). ^{13}C-NMR: 145.9 (*s*, 3 arom. C); 129.9 (*d*, 3 arom. C); 127.4 (*d*, 6 arom. C); 125.9 (*d*, 6 arom. C); 81.0 (*d*, SiCH); 61.2 (*s*, Ph_3C); 60.4 (*q*, MeO); –2.0, –6.3 (2*q*, Me_2Si). ESI-MS: 369 (10, $[M+Na]^+$); 303 (100, $[M–43]^+$).

(1'*S*,2*S*)- and (1'*R*,2*S*)-2-[(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silyloxy]-1,1,2-tri-phenylethanol (80a and 80b)



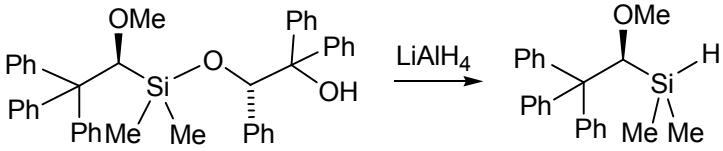
A soln. of **69** (3.46 g, 10.00 mmol) in CH_2Cl_2 (150.0 mL) was cooled to –78 °C and Br_2 (0.54 mL, 10.05 mmol) was added dropwise. The mixture was stirred for 10 min, the cooling bath was removed, and the solvent evaporated at 23 °C at reduced pressure. The residue was dissolved in CH_2Cl_2 (200.0 mL) and the mixture cooled to 0 °C. NEt_3 (2.8 mL, 20.00 mmol), (*S*)-1,1,2-triphenylethane-1,2-diol (3.21 g, 10.50 mmol), and DMAP (122.1 mg, 1.00 mmol) were added. The mixture was stirred at 23°C for 1 h, quenched with H_2O (100 mL), and the two layers were separated. The aq. phase was extracted with Et_2O (2 x 200 mL) and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2; toluene) afforded **80a** (200.8 mg, 0.36 mmol, 36%) and subsequently **80b** (217.3 mg, 0.37 mmol, 38%) as a colorless oils.

80a: $[\alpha]_D^{25}$ = –25.8 (c = 1.23, $CHCl_3$). IR: 3420*s* (br), 3050*s*, 2920*s*, 2860*s*, 2820*s*, 1490*s*, 1442*s*, 1250*s*, 1115*s*, 1095*s*, 1080*s*, 935*s*. ^{1}H-NMR: 7.73–7.69, 7.39–6.97 (2*m*, 30 arom. H); 5.52 (*s*, SiOCH); 4.23 (*s*, SiCH); 3.39 (br.*s*, OH); 3.07 (*s*, MeO); –0.25, –0.79 (2*s*, Me_2Si). ^{13}C-NMR: 146.1, 145.8, 143.0, 139.6, 129.0, 128.2 (6*s*, 6 arom. C); 130.0, 128.8, 128.0, 127.5, 127.4, 127.3, (6*d*, 6 arom. C); 127.2, 127.0, 126.4, 126.3, 125.9, 125.3 (6*d*, 6 x 4 arom. C); 83.7 (*d*, SiCH); 81.0 (*s*, (OH)C); 80.1 (*d*, SiOCH); 60.7 (*s*, Ph_3C); 60.6 (*q*, MeO); 0.0, –1.9 (2*q*, Me_2Si). ESI-MS: 657 ([*M*+Na]$^+$).

80b: $[\alpha]_D^{25}$ = –156.2 (c = 1.13, $CHCl_3$). IR: 3420br.*s*, 3048*s*, 2920*s*, 2860*s*, 2820*s*, 1490*s*, 1440*s*, 1247*s*, 1114*s*, 1095*s*, 1080*s*, 935*s*. ^{1}H-NMR: 7.80–7.75, 7.47–7.00 (2*m*, 30 arom. H); 5.55 (*s*, 1H, SiOCH); 4.19 (*s*, 1H, SiCH); 3.47 (br.*s*, 1H, OH); 3.11 (*s*, 3H, MeO); –0.40, –0.72 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 146.2, 145.8, 142.9, 139.6, 129.0, 128.2 (6*s*, 6 arom. C); 130.0, 128.8, 128.1, 127.4, 127.3, 127.1 (6*d*, 6 arom. C); 127.2, 127.0, 126.9, 126.4, 125.9, 125.3 (6*d*, 6 x 4 arom. C); 83.3 (*d*, SiCH); 81.0 (*s*, (OH)C); 80.3 (*d*, SiOCH); 60.9 (*s*, Ph_3C); 60.5 (*q*, MeO); –0.3, –1.3 (2*q*, Me_2Si). ESI-MS: 657 ([*M*+Na]$^+$).

The diastereomeric purities of **80a** and **80b** (> 99.9%) were checked by ^{1}H-NMR.

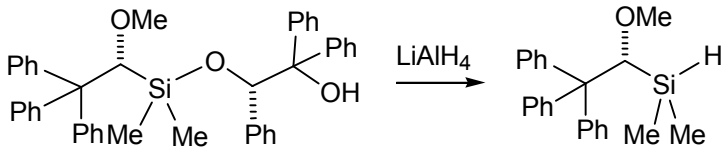
(+)-(*S*)-(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silane (69a)



80a **69a**

A soln. of **80a** (558.2 mg, 1.00 mmol) in CH_2Cl_2 (15.0 mL) was cooled to 0° C. A soln. of $LiAlH_4$ (1.0 M, 1.5 mL, 1.50 mmol) in Et_2O was added and the mixture stirred for 1 h at 23 °C. The excess of $LiAlH_4$ was neutralized with an aq. soln. of H_2SO_4 (10%), the layers were separated and the aq. phase was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography (SiO_2, hexane/EtOAc 50:1) to afford (*S*)-**69a** (341.7 mg, 0.98 mmol, 99%) as a colorless oil. $[\alpha]_D^{25}$(**69a**) = +27.0 (c = 0.98, $CHCl_3$).

(–)-(*R*)-(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silane (69b)



80b **69b**

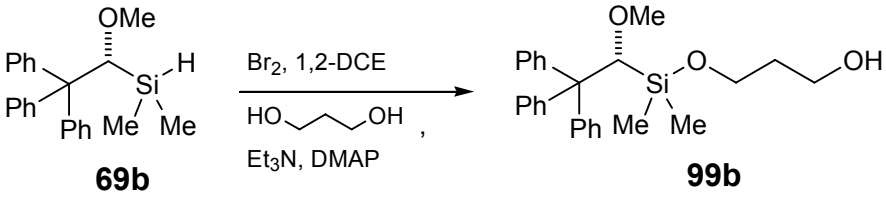
The same procedure of the previous reaction was followed to reduce **80b** to **69b**. $[\alpha]_D^{25}$(**69b**) = –30.1 (c = 1.31, $CHCl_3$).

5.3. Stereoselective reactions with silylethers

5.3.1. Nucleophilic additions to β-silyloxyaldehydes

5.3.1.1. Preparation of the subtrates and reactions

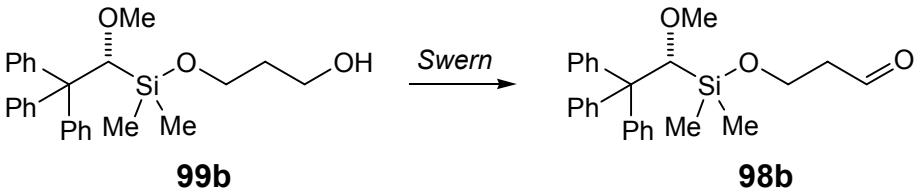
(1'*R*)-3-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilanoxy]propan-1-ol (99b)



69b **99b**

A soln. of **69b** (346.2 mg, 1.0 mmol) in CH_2Cl_2 (15.0 mL) was cooled to –78 °C, and Br_2 (0.054 mL, 1.05 mmol) was added dropwise. The cooling bath was removed, and the solvent evaporated under reduced pressure. The residual was then dissolved in CH_2Cl_2 (20.0 mL), the mixture cooled to 0 °C and NEt_3 (0.28 mL, 2.0 mmol), propane-1,3-diol (152.2 mg, 2 mmol), and DMAP (12.2 mg, 0.01 mmol) were added. The mixture was stirred at 23 °C for 1 h and quenched with H_2O (10 mL). The two layers were separated, the aq. phase extracted with Et_2O (2 x 20 mL), and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography of the residue (SiO_2, hexane/EtOAc 15:1) afforded **99b** as a colorless oil (403.2 mg, 0.96 mmol, 96%). $[\alpha]_D^{25}$(**99b**) = –72.8 (c = 1.20, $CHCl_3$). IR: 3417br.*s*, 3046*s*, 2931*s*, 2854*s*, 2829*s*, 1492*s*, 1444*s*, 1268*s*, 1106*s*, 1097*s*, 1071*s*, 941*s*. ^{1}H-NMR: 7.35–7.09 (*m*, 15 arom. H); 4.48 (*s*, 1H, SiCH); 4.20–3.96 (*m*, 4H, SiOC*H*$_2$CH$_2$C*H*$_2$OH); 3.67 (*s*, 3H, MeO); 2.41 (*s*, 1H, OH); 2.11–2.01 (*m*, 2H, SiOCH$_2$C*H*$_2$); 0.36, –0.01 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 147.8 (*s*, arom. C); 131.9, 129.2, 127.8 (3*d*, arom. C); 85.4 (*d*, SiCH); 63.6, 63.5 (2*t*, SiO*C*H$_2$CH$_2$*C*H$_2$OH); 62.9 (*q*, MeO); 62.6 (*s*, Ph_3C); 36.2 (*t*, SiOCH$_2$*C*H$_2$); –1.0, –2.0 (2*q*, Me_2Si). CI-MS: 438 (16, [*M*+NH_4]$^+$); 271 (100).

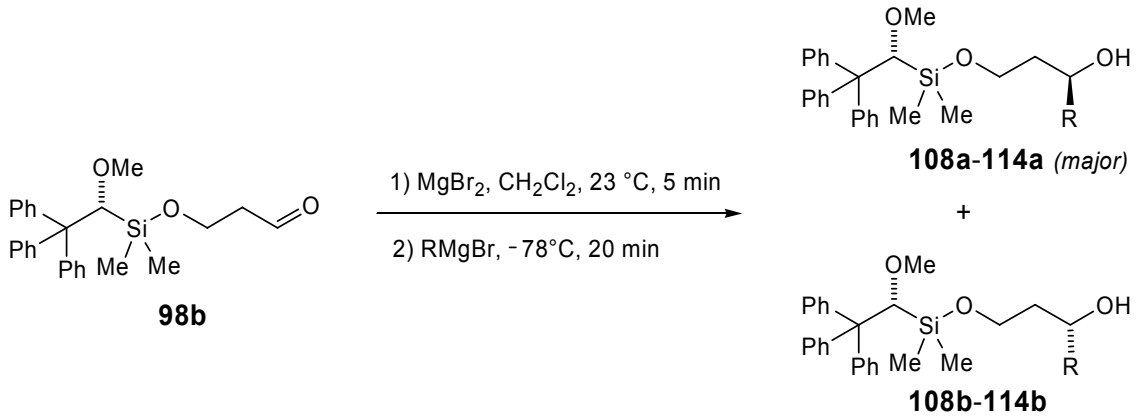
(1'*R*)-3-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilanoxy]propionaldehyde (98b)



99b **98b**

A soln. of $(COCl)_2$ (0.25 mL, 2.95 mmol) in CH_2Cl_2 (50.0 mL) was cooled to –78 °C, then DMSO (0.26 mL, 3.69 mmol) added and the mixture stirred for 30 min. After addition of a soln. of **99b** (1.00 g, 2.46 mmol) in CH_2Cl_2 (15.0 mL), and 30 min more of stirring at –78 °C, NEt_3 (1.1 mL, 7.87 mmol) was added, and the temperature was allowed to rise to 23 °C. The reaction was quenched with H_2O (30 mL), the two layers were separated, the aq. phase extracted with Et_2O (2 x 20 mL), and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2; hexane/EtOAc 10:1) afforded **98b** (0.96 mg, 2.36 mmol, 96%) as a colorless oil. $[\alpha]_D^{25}$(**98b**) = –81.6 (c = 1.20, $CHCl_3$). IR: 2918*s*, 2856*s*, 1753*s*, 1491*s*, 1443*s*, 1239*s*, 1129*s*, 1088*s*, 1081*s*, 941*s*. ^{1}H-NMR: 9.76 (*s*, CHO); 743–7.27 (*m*, 15 arom. H); 4.51 (*s*, 1H, SiCH); 3.97–3.91 (*m*, 2H, $SiOCH_2$); 3.42 (*s*, 3H, MeO); 2.67–2.59 (*m*, 2H, CH_2CHO) 0.17, –0.26 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 203.6 (*d*, CHO); 147.8 (*s*, 3 arom. C); 131.9, 129.1, 127.8 (3*d*, 15 arom. C); 85.2 (*d*, SiCH); 62.7 (*t*, $SiOCH_2$); 62.5 (*q*, MeO); 58.5 (*s*, Ph_3C); 48.1 (*t*, CH_2CHO); 0.4, 0.0 (2*q*, Me_2Si). ESI-MS: 473 (100, $[M+CH_3OH+Na]^+$); 441 (15, $[M+Na]^+$).

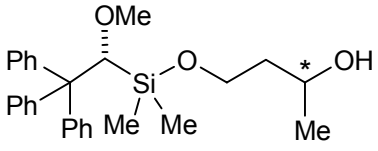
General procedure for the stereospecific additions of *Grignard* reagents:



A soln. of $MgBr_2$ in Et_2O (1.00 M, 0.40 mL, 0.40 mmol) was added to a soln. of **98b** (0.10 mmol) in CH_2Cl_2 (1.00 mL). The mixture was cooled to –78 °C and a soln. of *Grignard* reagent in CH_2Cl_2 (1.0 M, 0.30 mL, 0.30 mmol) was added dropwise. After 20 min the reaction was quenched with a sat. aq. soln. of NH_4Cl (5 mL). The two layers were separated, and the aq. phase was extracted with Et_2O (2 x 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure.

All the crude mixtures were analyzed by NMR spectroscopy and then purified by flash silica gel chromatography (hexane/EtOAc 10:1). Diastereoselectivities were established by integration of the signals correspondent to the Si*Me*$_2$ of the two diastereoisomers' absorptions in ^{1}H-NMR. Analytical data refer to the major isomer.

(1'*R*,2*R*)- and (1'*R*,2*S*)-4-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy] butan-2-ol (108a and 108b)

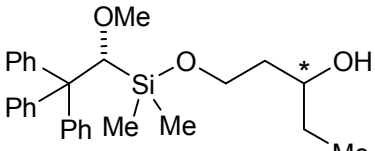


108a and **108b**

This compound was prepared according to the general procedure, adding MeMgBr to **98b** (41.8 mg, 0.10 mmol). After purification, a mixture of **108a** and **108b** (41.7 mg, 0.096 mmol, 96%, dr 93:7) was obtained as a colorless oil. IR: 3439br.*m*, 3045*s*, 2976*s*, 2910*s*, 2876*s*, 2809*s*, 1488*s*, 1441*s*, 1247*s*, 1089*s*, 1077*s*.

^{1}H-NMR: 7.46–7.31 (*m*, 15 arom. H); 4.61 (*s*, 1H, SiCH); 4.18–4.09 (*m*, 1H, C*H*OH); 3.94–3.71 (*m*, 2H, $SiOCH_2$); 3.48 (*s*, 3H, MeO); 2.72 (br.*s*, 1H, OH); 1.73–1.67 (*m*, 2H, CH_2CHO); 1.39–1.34 (*d*, *J* = 6.5, 3H, *Me*(OH)C); 0.01, –0.13 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.2 (*s*, 3 arom. C); 129.6, 128.1, 125.4 (3*d*, 15 arom. C); 83.1 (*d*, SiCH); 67.7 (*t*, $SiOCH_2$); 67.4 (*d*, (OH)CH); 60.6 (*q*, MeO); 60.3 (*s*, Ph_3C); 35.7 (*t*, $SiOCH_2CH_2$); 16.9 (*q*, *Me*(OH)CH); –0.1, –1.8 (2*q*, Me_2Si). ESI-MS: 457 ([*M*+Na]$^+$).

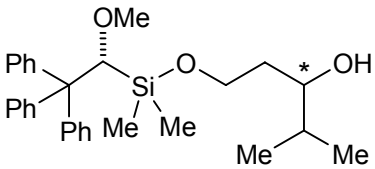
(1'*R*,3*R*)- and (1'*R*,3*S*)-1-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy] hexan-3-ol (109a and 109b)



109a and **109b**

This compound was prepared according to the general procedure, adding EtMgBr to **98b** (41.8 mg, 0.10 mmol). After purification, a mixture of **109a** and **109b** (42.6 mg, 0.095 mmol, 95%, dr 93:7) was obtained as a colorless oil. IR: 3456br.*m*, 3062*s*, 2971*s*, 2926*s*, 2891*s*, 2823*s*, 1588*s*, 1491*s*, 1455*s*, 1253*s*, 1099*s*, 1084*s*. ^{1}H-NMR: 7.48–7.40 (*m*, 15 arom. H); 4.52 (*s*, 1H, SiCH); 3.98–3.74 (*m*, 3H, $SiOCH_2CH_2CH$); 3.49 (*s*, 3H, MeO); 2.21 (br.*s*, 1H, OH); 1.81–1.75 (*m*, 2H, OCH_2CH_2); 1.70–1.62 (*m*, 2H, $MeCH_2$); 1.21–1.03 (*m*, 3H, *Me*CH_2); 0.01, –0.18 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.2 (*s*, 3 arom. C); 129.6, 128.1, 125.4 (3*d*, 15 arom. C); 83.6 (*d*, SiCH); 71.9 (*d*, (OH)CH); 66.9 (*t*, $SiOCH_2$); 61.8 (*q*, MeO); 61.5 (*s*, Ph_3C); 36.1 (*t*, $SiOCH_2CH_2$); 28.4 (*t*, $MeCH_2$); 10.2 (*q*, *Me*CH_2); –1.0, –2.2 (2*q*, Me_2Si). ESI-MS: 471 ([*M*+Na]$^+$).

(1'*R*,3*R*)- and (1'*R*,3*S*)-1-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]-4-methylpentan-3-ol (110a and 110b)

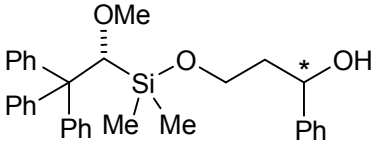


110a and **110b**

This compound was prepared according to the general procedure, adding *i*PrMgBr to **98b** (41.8 mg, 0.10 mmol). After purification, a mixture of **110a** and **110b** (44.5 mg, 0.096 mmol, 96%, dr 91:9) was obtained as a colorless oil.

IR: 3510br.*m*, 3064*s*, 2962*s*, 2927*s*, 2865*s*, 1490*s*, 1456*s*, 1254*s*, 1094*s*, 1087*s*. ^{1}H-NMR: 7.67–7.48 (*m*, 15 arom. H); 4.59 (*s*, 1H, SiCH); 4.28–3.99 (*m*, 2H, $SiOCH_2$); 3.88–3.79 (*m*, 1H, C*H*OH); 3.64 (*s*, 3H, MeO); 3.26 (br.*s*, 1H, OH); 2.09 (br.*s*, 1H, OH); 2.10–1.78 (*m*, 3H, $CH_2CHCHMe_2$); 1.63–1.55 (*m*, 1H, Me_2CH); 1.28, 1.19 (2*d*, *J* = 6.3, 6H, 2 *Me*CH); 0.19, 0.01 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 146.9 (*s*, 3 arom. C); 131.1, 128.3, 127.0 (3*d*, 15 arom. C); 84.6 (*d*, SiCH); 78.4 (*d*, (OH)CH), 63.9 (*t*, $SiOCH_2$); 62.1 (*q*, MeO); 61.7 (*s*, Ph_3C); 36.5 (*d*, Me_2CH); 34.7 (*t*, $SiOCH_2CH_2$); 19.4, 18.7 (2*q*, 2 *Me*CH); –0.8, –0.9 (2*q*, Me_2Si). ESI-MS: 485 ([*M*+Na]$^+$).

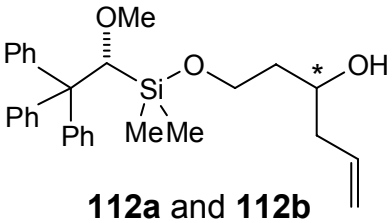
(1'*R*,1*R*)- and (1'*R*,1*S*)- [(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]-1-phenylpropanol (111a and 111b)



111a and **111b**

This compound was prepared according to the general procedure, adding PhMgBr to **98b** (41.8 mg, 0.10 mmol). After purification, a mixture of **111a** and **111b** (45.2 mg, 0.091 mmol, 91%, dr 92:8) was obtained as a yellowish oil. **111a** was separated then from **111b** by SiO_2 chromatography on a preparative TLC (hexane/EtOAc 15:1). IR: 3428br.*m*, 3046*s*, 2950*s*, 2918*s*, 2867*s*, 2841*s*, 1483*s*, 1445*s*, 1247*s*, 1101*s*, 1076*s*. ^{1}H-NMR: 7.63–7.48 (*m*, 20 arom. H); 5.11–5.07 (*m*, 1H, (OH)C*H*); 4.69 (*s*, 1H, SiCH); 4.09–3.97 (*m*, 2H, $SiOCH_2$); 3.68 (*s*, 3H, MeO); 2.47 (br.*s*, 1H, OH); 2.26–2.18 (*m*, 2H, $SiOCH_2CH_2$); 0.19, 0.02 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 144.2 (*s*, 3 arom. C); 138.8 (*s*, 1 arom. C); 130.0, 128.4, 127.3, 127.0, 126.5, 126.2 (6*d*, 20 arom. C); 84.6 (*d*, SiCH); 74.1 (*d*, (OH)CH); 68.4 (*t*, $SiOCH_2$); 61.2 (*q*, MeO); 60.7 (*s*, Ph_3C); 34.7 (*t*, $SiOCH_2CH_2$); –1.0, –2.1 (2*q*, Me_2Si). ESI-MS: 519 ([*M*+Na]$^+$).

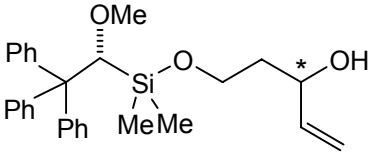
(1'*R*,3*R*)- and (1'*R*,3*S*)-1-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]hex-5-en-3-ol (112a and 112b)



112a and **112b**

This compound was prepared according to the general procedure, adding AllylMgBr to **98b** (41.8 mg, 0.10 mmol). After purification, a mixture of **112a** and **112b** (45.1 mg, 0.098 mmol, 98%, dr 94:6) was obtained as colorless oil. IR: 3452br.*m*, 3053*s*, 2979*s*, 2924*s*, 2887*s*, 2823*s*, 1495*s*, 1451*s*, 1253*s*, 1103*s*, 1084*s*. ^{1}H-NMR: 7.48–7.31 (*m*, 15 arom. H); 6.10–5.94 (*m*, 1H, *H*C=CH$_2$); 5.37–5.26 (*m*, 2H, HC=C*H*$_2$); 4.55 (*s*, 1H, SiCH); 4.06–3.81 (*m*, 3H, SiOC*H*$_2$CH$_2$C*H*); 3.50 (*s*, 3H, MeO); 3.10 (br. *s*, 3.12, OH); 2.45–2.38 (*m*, 2H, C*H*$_2$CH=CH$_2$); 1.74–1.35 (*m*, 2H, SiOCH$_2$C*H*$_2$); 0.02, –0.16 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 146.1 (*s*, 3 arom. C); 134.8 (*d*, H*C*=CH$_2$); 130.1, 127.3, 126.0 (3*d*, 15 arom. C); 117.1 (*t*, HC=*C*H$_2$); 83.6 (*d*, SiCH); 70.8 (*d*, (OH)CH); 63.1 (*t*, SiOCH$_2$); 62.9 (*q*, MeO); 62.7 (*s*, Ph$_3$*C*); 37.4 (*t*, *C*H$_2$C=C); 35.6 (*t*, SiOCH$_2$*C*H$_2$); 0.0, –0.1 (2*q*, Me$_2$Si). ESI-MS: 483 ([*M*+Na]$^+$).

(1'*R*,3*R*)- and (1'*R*,3*S*)-5-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy] pent-1-en-3-ol (113a and 113b)

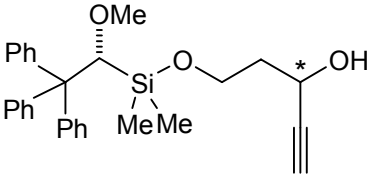


113a and **113b**

This compound was prepared according to the general procedure, adding VinylMgBr to **98b** (43.2 mg, 0.10 mmol). After purification, a mixture of **113a** and **113b** (41.5 mg, 0.093 mmol, 93%, dr 94:6) was obtained as a colorless oil. IR: 3446br.*m*, 3041*s*, 2975*s*, 2920*s*, 2878*s*, 2816*s*, 1491*s*, 1446*s*, 1249*s*, 1095*s*, 1080*s*. ^{1}H-NMR: 7.67–7.47 (*m*, 15 arom. H); 6.29–6.14 (*m*, 1H, *H*C=CH$_2$); 5.13–5.49 (*m*, 2H, HC=C*H*$_2$); 4.67 (*s*, 1H, SiCH); 4.12–3.97 (*m*, 3H, SiOC*H*$_2$CH$_2$C*H*); 3.68 (*s*, 3H, MeO); 3.25 (br. *s*, 3.12, OH); 2.09–1.94 (*m*, 2H, SiOCH$_2$C*H*$_2$); 0.19, –0.01 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 147.8 (*s*, 3 arom. C); 142.7 (*d*, H*C*=CH$_2$); 131.8, 129.5, 127.9 (3*d*, 15 arom. C); 116.2 (*t*, HC=*C*H$_2$); 85.6 (*d*, SiCH);

73.7 (*d*, (OH)CH); 63.0 (*q*, MeO); 62.7 (*t*, $SiOCH_2$); 62.7 (*s*, Ph_3C); 40.4 (*t*, $SiOCH_2CH_2$); 0.9, 0.0 (2*q*, Me_2Si). ESI-MS: 469 ($[M+Na]^+$).

(1'*R*,3*R*)- and (1'*R*,3*S*)-5-[(1-Methoxy-2,2,2-triphenyl-ethyl)-dimethyl-silyloxy]-pent-1-en-3-ol (114a and 114b)

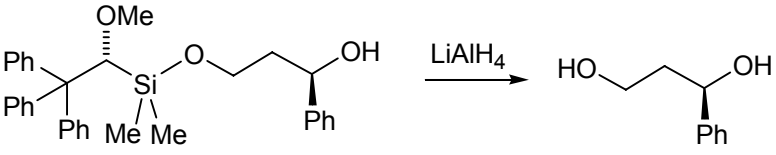


114a and **114b**

This compound was prepared according to the general procedure, adding EthynylMgBr to **98b** (44.8 mg, 0.10 mmol). After purification, a mixture of **114a** and **114b** (43.2 mg, 0.097 mmol, 97%, dr 57:43) was obtained as a colorless oil. IR: 3395br.*s*, 3050*s*, 2970*s*, 2922*s*, 2862*s*, 2550*s*, 1490*s*, 1455*s*, 1250*s*, 1115*s*, 1095*s*, 1085*s*. ^{1}H-NMR: 7.31–7.14 (*m*, 15 arom. H); 4.23 (*s*, 1H, SiCH); 4.24 (br.*m*, 1H, (OH)C*H*); 3.61–3.43 (*m*, 2H, $SiOCH_2$); 3.33 (*s*, 3H, MeO); 2.38 (br.*s*, 1H, OH); 2.37 (*d*, *J* = 2.0, CCH); 1.74–1.35 (*m*, 2H, $SiOCH_2CH_2$); –0.01, –0.05, (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.8, (*s*, arom. C); 130.1, 127.4, 126.0 (3*d*, arom. C); 83.1 (*d*, SiCH); 81.8 (*s*, *C*CH); 74.3 (*d*, C*C*H); 66.3 (*t*, $SiOCH_2$); 62.7 (*d*, (OH)CH); 61.2 (*q*, MeO); 60.7 (*s*, Ph_3C); 35.6 (*t*, $SiOCH_2CH_2$); –0.9, –2.2 (2*q*, Me_2Si). ESI-MS: 553 ($[M+Na]^+$).

5.3.1.2. Stereochemical assignments

(*R*)-1-Phenylpropane-1,3-diol (121)

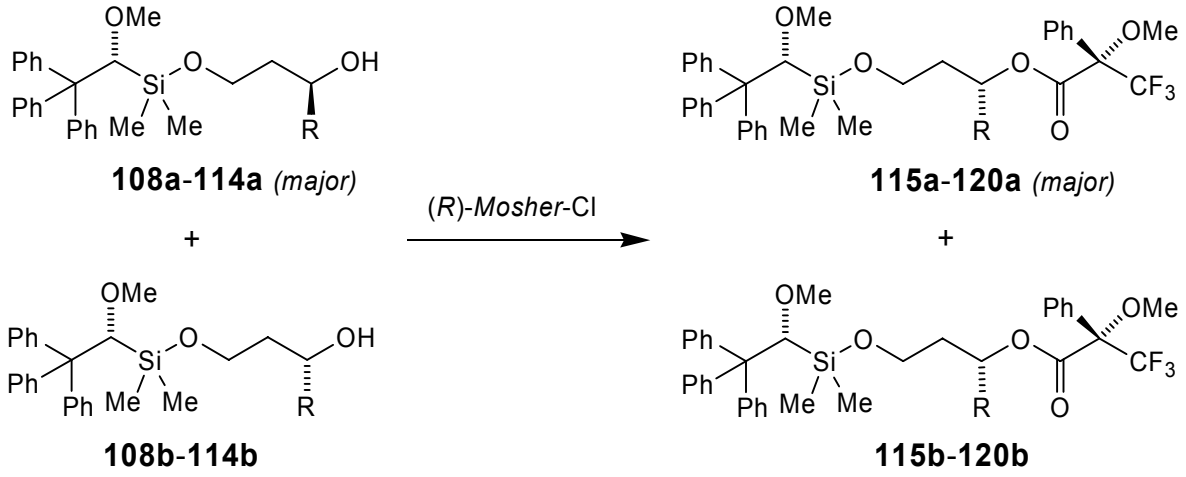


111a **121**

A soln. of $LiAlH_4$ in Et_2O (1.0 M, 0.3 mL, 0.30 mmol) was added to a soln. of **111a** (99.2 mg, 0.20 mmol, de > 99.9% checked by ^{1}H-NMR) in THF (1.0 mL) at 0 °C. After 30 min, a sat. aq. soln. of NH_4Cl (2 mL) was added, the two layers were separated and the aq. phase was extracted with Et_2O (2 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by flash

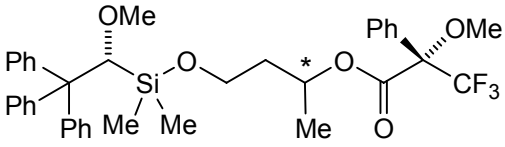
chromatography (SiO_2; hexane/EtOAc 40:1 to 5:1) afforded (*R*)-MOTES-H **69b** (67.8 mg, 0.196 mmol, 96%) and subsequently **121** (29.8 mg, 0.19 mmol, 96%) as a slightly yellowish oil. $[\alpha]_D^{25}$ = +66.3 (c = 0.90, $CHCl_3$) [(*R*)-**121**: $[\alpha]_D^{25}$ = +69.0 (c = 1.00, $CHCl_3$), (*S*)-**121**: $[\alpha]_D^{25}$ = –63.3 (c = 1.0, $CHCl_3$)], confirming the configuration of **111a** as shown above. Analytical data in agreement with literature.[75, 76]

General procedure for the esterification with (–)-(*R*)-*Mosher* acid chloride:



A soln. of the desired mixture (0.34 mmol) in pyridine (1.0 mL) was added at 23 °C to a soln. of (*R*)-(2)-α-methoxy-α-(trifluoromethyl)phenylacetylchloride [(–)-(*R*)-*Mosher* acid chloride] (120.2 mg, 0.5 mmol) in CH_2Cl_2 (1.0 mL) and stirred. After 2 h, TMEDA (0.076 mL, 0.5 mmol) was added, and the reaction was quenched with H_2O (1.0 mL). The two layers were separated, and the aq. phase was extracted with Et_2O (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography (SiO_2; hexane/EtOAc 5:1). Absolute configurations were established by configurational correlation via ^{1}H-NMR spectroscopy. Analytical data refer to the major isomers.

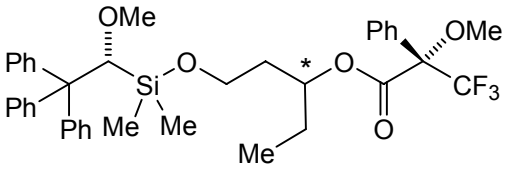
(1'*R*,2*S*)-3-{[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]-1-methyl propyl}-3,3,3-trifluoro-2-methoxy-2-phenylpropionate (115a and 115b)



115a and **115b**

108a and **108b** (147.6 mg, 0.34 mmol) were derivatized according to general procedure. After chromatography a mixture of **115a** and **115b** (212.2 mg, 0.33 mmol, 97%) was obtained as a colorless oil. ^{1}H-NMR: 7.75–7.30 (*m*, 20 arom. H); 5.49–5.38 (*m*, 1H, OC*H*CH_2); 4.57 (*s*, 1H, SiCH); 3.73–3.67 (*m*, 5H, $SiOCH_2$ and CF_3COMe); 3.48 (*s*, 3H, MeOCSi); 2.09–1.95 (*m*, 2H, CH_2CH); 1.45 (*d*, *J* = 6.3, 3H, *Me*CH); 0.00, –0.24 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 167.4 (*s*, COO); 148.3, 147.5 (*s*, 4 arom. C); 134.6 (*q*, CF_3); 132.1, 131.6, 130.4, 129.4, 128.0, 127.6 (6*d*, 20 arom. C); 85.1 (*d*, SiCH); 79.9 (s, *C*CF_3); 74.8 (*d*, OCH); 62.2 (*q*, *Me*OCH); 61.6 (*q*, *Me*OCCF_3); 59.7 (*t*, $SiOCH_2$); 57.6 (*s*, Ph_3C); 36.4 (*t*, $SiOCH_2CH_2$); 19.7 (*q*, *Me*CH); 0.1, –0.5 (2*q*, Me_2Si). ^{19}F-NMR: –72.1 (*s*, 3F, CF_3).

(1'*R*,2*S*)-3-{[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]-1-ethylpropyl}-3,3,3-trifluoro-2-methoxy-2-phenylpropionate (116a and 116b)

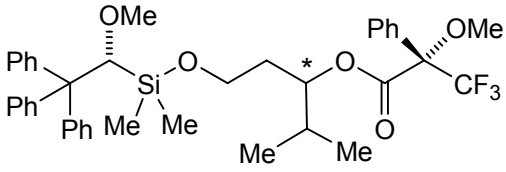


116a and **116b**

109a and **109b** (152.4 mg, 0.34 mmol) were derivatized according to general procedure. After chromatography a mixture of **116a** and **116b** (214.5 mg, 0.32 mmol, 95%) was obtained as a colorless oil. ^{1}H-NMR: 7.80–7.32 (*m*, 20 arom. H); 5.52–5.43 (*m*, 1H, OC*H*CH_2); 4.59 (*s*, 1H, SiCH); 3.76–3.70 (*m*, 5H, $SiOCH_2$ and CF_3COMe); 3.52 (*s*, 3H, MeOCSi); 2.08–1.70 (*m*, 4H, CH_2CHCH_2); 1.04 (*m*, 3H, *Me*CH_2); 0.01, –0.22 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 167.3 (*s*, COO); 148.1, 147.3 (*s*, 4 arom. C); 134.3 (*q*, CF_3); 131.9, 131.4, 130.1, 129.1, 127.7, 127.6 (6*d*, 20 arom. C); 84.8 (*d*, SiCH); 79.8 (s, *C*CF_3); 74.8 (*d*, OCH); 62.4 (*q*, *Me*OCH); 61.8 (*q*, *Me*OCCF_3); 59.4 (*t*, $SiOCH_2$); 57.3

(*s*, Ph_3C); 36.1 (*t*, $SiOCH_2CH_2$); 27.7 (*t*, $MeCH_2$) 9.7 (*q*, $MeCH_2$); 0.4, –0.2 (2*q*, Me_2Si). ^{19}F-NMR: –72.2 (*s*, 3F, CF_3).

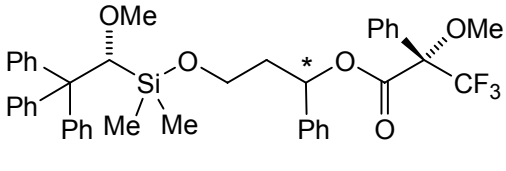
(1'*R*,2*S*)-3-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]ethyl-2-methyl propyl-3,3,3-trifluoro-2-methoxy-2-phenylpropionate (117a and 117b)



117a and **117b**

110a and **110b** (157.1 mg, 0.34 mmol) were derivatized according to general procedure. After chromatography a mixture of **117a** and **117b** (223.6 mg, 0.33 mmol, 97%) was obtained as a colorless oil. ^{1}H-NMR: 7.79–7.37 (*m*, 20 arom. H); 5.39–5.30 (*m*, 1H, OC*H*CH_2); 4.61 (*s*, 1H, SiCH); 3.77–3.64 (*m*, 5H, $SiOCH_2$ and CF_3COMe); 3.50 (*s*, 3H, MeOCSi); 2.21–1.82 (*m*, 3H, C*H*CHCH_2); 1.19, 1.01 (2*d*, *J* = 6.3, 6H, Me_2CH); 0.00, –0.21 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 167.0 (*s*, COO); 148.0, 147.6 (*s*, 4 arom. C); 134.6 (*q*, CF_3); 132.1, 131.6, 130.4, 129.4, 128.0, 127.6 (6*d*, 20 arom. C); 85.4 (*d*, SiCH); 80.7 (s, *C*CF_3); 74.9 (*d*, OCH); 62.0 (*q*, *Me*OCH); 61.8 (*q*, *Me*$OCCF_3$); 59.6 (*t*, $SiOCH_2$); 57.4 (*s*, Ph_3C); 36.6 (*t*, $SiOCH_2CH_2$); 33.3 (*d*, Me_2CH); 19.9 (*q*, Me_2CH); 0.2, –0.1 (2*q*, Me_2Si). ^{19}F-NMR: –71.8 (*s*, 3F, CF_3).

(1'*R*,2*S*)-3-{[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]-1phenylpropyl}-3,3,3-trifluoro-2-methoxy-2-phenylpropionate (118a and 118b)

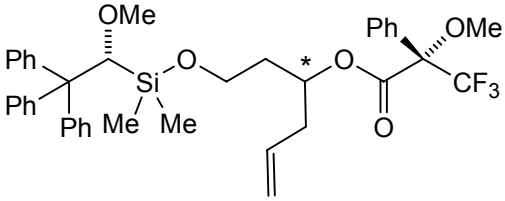


118a and **118b**

111a and **111b** (168.6 mg, 0.34 mmol) were derivatized according to general procedure. After chromatography a mixture of **118a** and **118b** (227.8 mg, 0.32 mmol, 95%) was obtained as a colorless oil. ^{1}H-NMR: 7.78–7.27 (*m*, 25 arom. H); 5.37–5.29 (*m*, 1H, OC*H*CH_2); 4.55 (*s*, 1H, SiCH); 3.77–3.64 (*m*, 5H, $SiOCH_2$ and CF_3COMe); 3.49 (*s*, 3H, MeOCSi); 2.13–1.89 (*m*, 2H, $SiOCH_2CH_2$); 0.06, –0.22 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 167.6 (*s*, COO); 143.9, 142.1, 138.7 (*s*, 5 arom. C); 133.8 (*q*, CF_3); 130.2, 128.6,

127.8, 127.4, 126.3, 126.4 (6*d*, 25 arom. C); 85.0 (*d*, SiCH); 76.8 (*s*, *C*CF_3); 73.5 (*d*, OCH); 62.8 (*q*, *Me*OCH); 62.4 (*q*, *Me*O*C*CF_3); 60.0 (*t*, $SiOCH_2$); 57.3 (*s*, Ph_3C); 38.9 (*t*, $SiOCH_2CH_2$); 0.6, 0.0 (2*q*, Me_2Si). ^{19}F-NMR: –72.2 (*s*, 3F, CF_3).

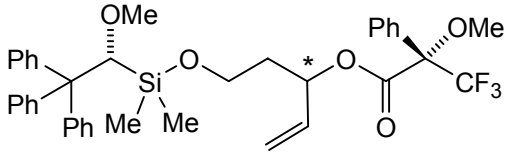
(1'*R*,2*S*)-3-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]ethylbut-3-enyl-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid ester (119a and 119b)



119a and **119b**

112a and **112b** (156.5 mg, 0.34 mmol) were derivatized according to general procedure. After chromatography a mixture of **119a** and **119b** (218.3 mg, 0.32 mmol, 95%) was obtained as a colorless oil. ^{1}H-NMR: 7.77–7.31 (*m*, 20 arom. H); 6.90–5.77 (*m*, 1H, C*H*=CH_2); 5.56–5.17 (*m*, 3H, C*H*CH_2CH=CH_2); 4.59 (*s*, 1H, SiCH); 3.76–3.67 (*m*, 5H, $SiOCH_2$ and CF_3COMe); 3.49 (*s*, 3H, MeOCSi); 2.68–2.52 (*m*, 2H, CHCH_2CHO); 2.09–1.88 (*m*, 2H, $SiOCH_2CH_2$); 0.03, –0.21 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 167.1 (*s*, COO); 147.2, 145.3 (2*s*, 4 arom. C); 136.5 (*d*, H*C*=CH_2); 133.9 (*q*, CF_3); 132.2, 131.6, 130.1, 129.3, 129.2, 127.6 (6*d*, 20 arom. C); 120.8 (*t*, HC=*C*H_2); 84.5 (*d*, SiCH); 76.6 (s, *C*CF_3); 74.9 (*d*, OCH); 62.0 (*q*, *Me*OCH); 61.8 (*q*, *Me*O*C*CF_3); 59.6 (*t*, $SiOCH_2$); 56.5 (*s*, Ph_3C); 39.3 (*t*, $SiOCH_2CH_2$); 37.3 (*t*, OCH*C*H_2CH); 0.0, –0.8 (2*q*, Me_2Si). ^{19}F-NMR: –71.9 (*s*, 3F, CF_3).

(1'*R*,2*S*)-3-[(1-Methoxy-2,2,2-triphenylethyl)-dimethylsilanyloxy]ethylprop-2-enyl-3,3,3-trifluoro-2-methoxy-2-phenylpropionate(120a and 120b)



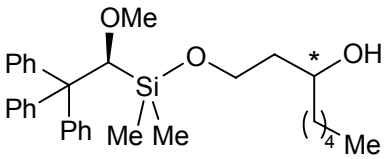
120a and **120b**

113a and **113b** (151.7 mg, 0.34 mmol) were derivatized according to general procedure. After chromatography a mixture of **120a** and **120b** (220.4 mg, 0.33 mmol, 98%) was obtained as a colorless oil. ^{1}H-NMR: 7.71–7.29 (*m*, 20 arom. H); 6.09–5.71 (*m*, 2H, C*HCH*=CH_2); 5.58–5.36 (*m*, 2H, HC=CH_2); 4.58 (*s*, 1H, SiCH); 3.71 (*s*, 3H, CF_3COMe); 3.70–3.67

(*m*, 2H, SiOCH_2); 3.49 (*s*, 3H, MeOCSi); 2.13–1.89 (*m*, 2H, SiOCH$_2$CH_2); 0.06, –0.22 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 167.2 (*s*, COO); 148.0, 147.1 (2*s*, 4 arom. C); 136.8 (*d*, H*C*=CH$_2$); 133.8 (*q*, CF_3); 132.0, 131.8, 130.2, 129.5, 129.2, 127.9 (6*d*, 20 arom. C); 120.4 (*t*, HC=*C*H$_2$); 85.3 (*d*, SiCH); 76.7 (*s*, *C*CF_3); 73.7 (*d*, OCH); 62.8 (*q*, *Me*OCH); 62.5 (*q*, *Me*O*C*CF_3); 60.0 (*t*, SiO*C*H$_2$); 57.3 (*s*, Ph_3C); 38.9 (*t*, SiOCH$_2$*C*H$_2$); 0.6, 0.0 (2*q*, Me_2Si). ^{19}F-NMR: –72.1 (*s*, 3F, CF_3).

5.3.1.3 Enantioselective synthesis of (*R*)-1-Octane-1,3-diol

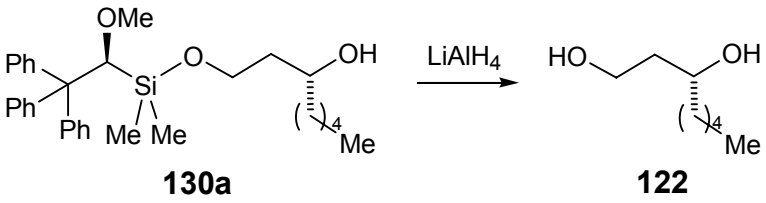
(1'*S*,3*S*)- and (1'*S*,3*R*)-1-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy] octan-3-ol (130a and 130b)



130a and **130b**

A soln. of $MgBr_2$ in Et_2O (1.00 M, 0.40 mL, 0.40 mmol) was added to a soln. of **98a** (41.8 mg, 0.10 mmol) in CH_2Cl_2 (5.00 mL). The mixture was cooled to –78 °C and a soln. of Pentyl MgBr in Et_2O (2.0 M, 0.15 mL, 0.30 mmol) was added dropwise. After 20 min the reaction was quenched with a sat. aq. soln. of NH_4Cl (5 mL). The two layers were separated, and the aq. phase was extracted with Et_2O (2 x 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. A mixture of **130a** and **130b** (45.5 mg, 0.096 mmol, 96%, dr 94:6) was obtained as a colorless oil. **130a** was separated then from **130b** by SiO_2 chromatography on a preparative TLC (hexane/EtOAc 15:1). IR: 3450br.*m*, 3062*s*, 2971*s*, 2926*s*, 2891*s*, 2823*s*, 1588*s*, 1491*s*, 1455*s*, 1253*s*, 1099*s*, 1084*s*. ^{1}H-NMR: 7.49–7.40 (*m*, 15 arom. H); 4.51 (*s*, 1H, SiCH); 4.02–3.89 (*m*, 3H, SiOCH_2CH$_2$C*H*); 3.50 (*s*, 3H, MeO); 3.11 (br.*s*, 1H, OH); 1.71–1.62 (*m*, 2H, OCH$_2$CH_2); 1.62–1.40 (*m*, 10H, OCH$_2$CH_2, Me(CH_2)$_4$); 1.12–1.03 (*t*, 3H, *J* = 6,2, *Me*CH$_2$); 0.00, –1.16 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 146.8 (*s*, 3 arom. C); 131.0 (*d*, 3 arom. C); 128.3 (*d*, 6 arom. C); 126.9 (*d*, 6 arom. C); 84.5 (*d*, SiCH); 72.3 (*d*, (OH)CH); 62.6 (*t*, SiO*C*H$_2$); 62.2 (*q*, MeO); 61.6 (*s*, Ph_3C); 39.4, 38.4, 32.9, 26.2, 23.6 (5*t*, SiOCH$_2$*C*H$_2$, Me(*C*H$_2$)$_4$); 14.9 (*q*, *Me*CH$_2$); 0.0, –1.0 (2*q*, Me_2Si). ESI-MS: 513 ([*M*+Na]$^+$).

(*R*)-1-Octane-1,3-diol (122)



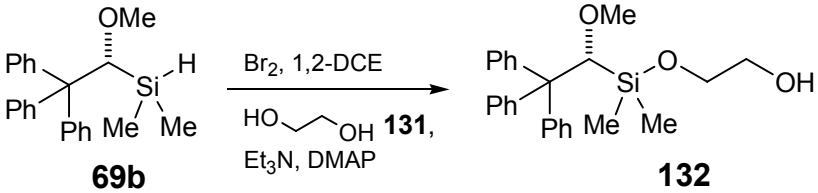
130a **122**

A soln. of $LiAlH_4$ in Et_2O (1.0 M, 0.3 mL, 0.30 mmol) was added to a soln. of **130a** (98.6 mg, 0.20 mmol) in THF (1.0 mL) at 0 °C. After 40 min, a sat. aq. soln. of NH_4Cl (2 mL) was added, the two layers were separated and the aq. phase was extracted with Et_2O (2 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by flash chromatography (SiO_2; hexane/EtOAc 30:1 to 5:1) afforded (*S*)-MOTES-H **69b** (34.7 mg, 0.196 mmol, 95%) and subsequently **122** (29.8 mg, 0.19 mmol, 95%) as a colorless oil. $[\alpha]_D^{25} = -9.1$ (c = 1.50, $CHCl_3$) [(*R*)-**122**: $[\alpha]_D^{25} = -11.2$ (c = 1.32, $CHCl_3$)], confirming the configuration as shown above. Analytical data in agreement with literature.[85]

5.3.2. Diels–Alder reactions

5.3.2.1. Preparation of the substrates and reactions

(1'*R*)-[(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silyloxy]ethanol (132)

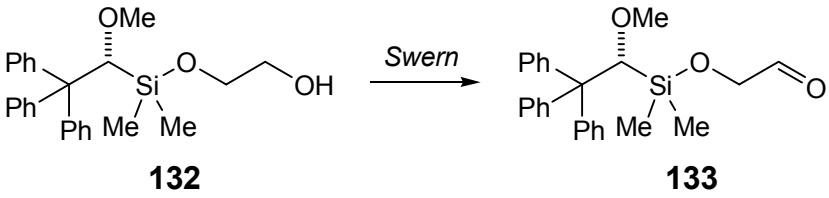


69b **132**

A soln. of **69b** (346.2 mg, 1.0 mmol) in CH_2Cl_2 (15.0 mL) was cooled to –78 °C, then Br_2 (0.054 mL, 1.05 mmol) was added drop wise. The cooling bath was removed, and the solvent evaporated under reduced pressure. The residual was dissolved in CH_2Cl_2 (20.0 mL), the mixture cooled to 0 °C, and NEt_3 (0.28 mL, 2.0 mmol), ethylene glycol (**131**) (124.4 mg, 2 mmol), and DMAP (12.2 mg, 0.01 mmol) were added. The mixture was stirred at 23 °C for 1 h, then quenched with H_2O (10 mL). The two layers were separated, the aq. phase was extracted with Et_2O (2 x 20 mL), and the

combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2; hexane/EtOAc 15:1) afforded **132** as a colorless oil (387.3 mg, 0.91 mmol, 91%). IR: 3420br.*s*, 3050*s*, 2920*s*, 2860*s*, 2820*s*, 1490*s*, 1442*s*, 1250*s*, 1115*s*, 1095*s*, 1080*s*, 935*s*. ^{1}H-NMR: 7.31–7.14 (*m*, 15 arom. H); 4.41 (*s*, 1H, SiCH); 3.55–3.44 (*m*, 4H, $SiOCH_2CH_2$); 3.33 (*s*, 3H, MeO); 1.72 (*s*, 1H, OH); –0.06, –0.37 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.9 (*s*, arom. C); 130.1, 127.3, 126.0 (3*d*, arom. C); 83.1 (*d*, SiCH); 65.8, 63.6 (2*t*, $SiOCH_2CH_2$); 61.1 (*q*, MeO); 60.8 (*s*, Ph_3C); –1.0, –2.0 (2*q*, Me_2Si). $[\alpha]_D^{25}$(**132**) = –74.1 (c = 1.25, $CHCl_3$). CI-MS: 424 (9, $[M+NH_4]^+$); 257 (100).

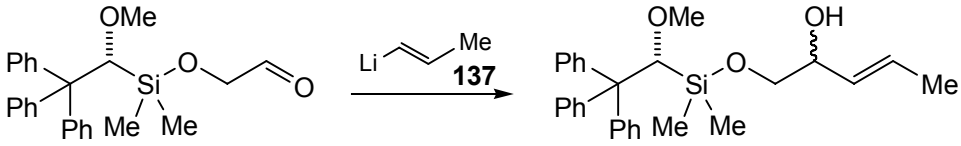
(1'*R*)-[(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silyloxy]acetaldehyd (133)



132 **133**

A soln. of $(COCl)_2$ (0.25 mL, 2.95 mmol) in CH_2Cl_2 (50.0 mL) was cooled to –78 °C, then DMSO (0.26 mL, 3.69 mmol) added and the mixture stirred for 30 min. After addition of a soln. of **132** (1.00 g, 2.46 mmol) in CH_2Cl_2 (15.0 mL), and 30 more min of stirring, NEt_3 (1.1 mL, 7.87 mmol) was added, the temperature risen till 23 °C and the reaction quenched with H_2O (30 mL). The two layers were then separated, the aq. phase extracted with Et_2O (2 x 20 mL), and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2; hexane/EtOAc 10:1) afforded **133 (**950.0 mg, 2.35 mmol, 95%) as a colorless dense oil. IR: 2920*s*, 2860*s*, 1748*s*, 1490*s*, 1445*s*, 1250*s*, 1125*s*, 1092*s*, 1080*s*, 935*s*. ^{1}H-NMR: 9.54 (*s*, CHO); 7.30–7.14 (*m*, 15 arom. H); 4.45 (*s*, 1H, SiCH); 3.98 (*s*, 2H, $SiOCH_2$); 3.33 (*s*, 3H, MeO); –0.12, –0.29 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 201.9 (*d*, CHO); 145.9 (*s*, 3 arom. C); 130.1, 127.4, 126.1 (3*d*, 15 arom. C); 83.7 (*d*, SiCH); 69.1 (*t*, $SiOCH_2$); 61.1 (*q*, MeO); 60.7 (*s*, Ph_3C); –1.2, –1.5 (2*q*, Me_2Si). ESI-MS: 459 (100, $[M+CH_3OH+Na]^+$); 427 (12, $[M+Na]^+$).

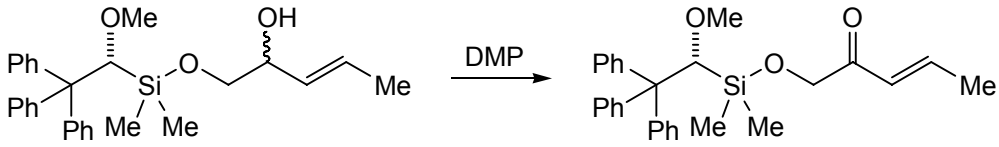
(1'*R*)-1-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]pent-3-en-2-ol (139)



133 **139**

Lithium (552.3 mg, 80.0 mmol) was added to a soln. of *trans*-1-bromopropene (**135**) (0.69 mL, 8.0 mmol, *E*/*Z* > 99%) in Et_2O (50.0 mL) at 0 °C and stirred for 2 h. The liquid phase was added to a soln. of **133** (800.5 mg, 1.99 mmol) in Et_2O (50.0 mL) at –78 °C, the reaction warmed up to –50 °C and stirred prolonged for 1 h. The cooling bath was removed, and H_2O (30 mL) added. The two layers were separated, the aq. phase was extracted with Et_2O (2 x 50 mL), and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2; hexane/EtOAc 15:1) afforded **139** (781.9 mg, 1.75 mmol, 88%). IR: 3448br.*m*, 2960*s*, 2928*s*, 1490*s*, 1447*s*, 1452*s*, 1245*s*, 1090*s*, 1078*s*, 822*s*. CI-MS: 271 (41); 106 (100). The NMR-data refer to the major isomer. ^{1}H-NMR: 7.38–7.12 (*m*, 15 arom. H); 5.81–5.50 (*m*, 1H, *H*C=CHCH$_3$); 5.42–5.30 (*m*, 1H, HC=C*H*CH$_3$); 4.45 (*s*, 1H, SiCH); 4.08–3.92 (*m*, 1H, (OH)C*H*); 3.50–3.42 (*m*, 2H, SiOCH$_2$); 3.36 (*s*, 3H, MeO); 2.30 (*s*, 1H, OH); 1.67–1.58 (*m*, 3H, CH$_3$CH); –0.03, –0.39 (*s*, 6H, Me$_2$Si). ^{13}C-NMR: 146.8 (*s*, 3 arom. C); 131.1 (*d*, H*C*=CHCH$_3$); 129.4, 128.5, 127.1 (3*d*, 15 arom. C); 126.9 (*t*, HC=*C*HCH$_3$); 84.0 (*d*, SiCH); 73.4 (*d*, (OH)C); 67.7 (*t*, SiOCH$_2$); 62.1 (*q*, MeO); 61.7 (*s*, Ph$_3$*C*); 18.7 (*q*, *C*H$_3$CH); –0.1, –1.2 (2*q*, Me$_2$Si).

(1'*R*)-1-[(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silyloxy]pent-3-en-2-on (141)

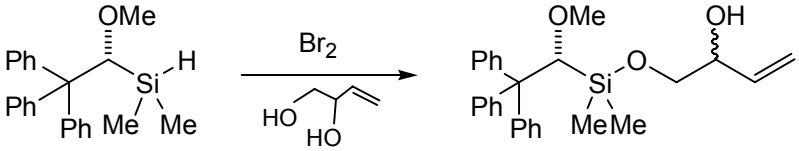


139 **141**

DMP (2.2 mL of a 15% soln. in CH_2Cl_2, 1.02 mmol) was added to a soln. of a mixture of **139** (303.2 mg, 0.68 mmol) in CH_2Cl_2

(7.0 mL) at 0 °C. After 10 min, the mixture was allowed to warm to 20 °C and stirred for 22 h. Then, MeOH (0.3 mL) was added. Evaporation of the combined organic fractions and column chromatography (SiO_2; hexane/EtOAc 20:1) afforded **141** (289.8 mg, 0.65 mmol, 96%) as a yellowish oil. IR: 2958*s*, 2924*s*, 1740*s*, 1700*s*, 1490*s*, 1445*s*, 1456*s*, 1250*s*, 1095*s*, 1080*s*, 830*s*. ^{1}H-NMR: 7.31–7.14 (*m*, 15 arom. H); 6.50 (*dd*, *J* = 10.3, 17.3, 1H, *H*C=CH$_2$); 6.27 (*dd*, *J* = 2.0, 17.3, 1H, HC=C*H*H); 5.74 (*dd*, *J* = 2.0, 10.3, 1H, HC=CH*H*); 4.46 (*s*, 1H, SiCH); 4.16 (*s*, SiOCH$_2$); 3.34 (*s*, 3H, MeO); –0.11, –0.32 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 198.3 (*s*, CO); 146.0 (*s*, 3 arom. C); 131.9 (*d*, H*C*=CH$_2$); 130.1, 127.4, 126.0 (3*d*, 15 arom. C); 128.6 (*t*, HC=*C*H$_2$); 83.7 (*d*, SiCH); 67.9 (*t*, SiOCH$_2$); 61.1 (*q*, MeO); 60.7 (*s*, Ph$_3$*C*); –1.3, –1.6 (2*q*, Me$_2$Si). $[\alpha]_D^{25}$(**141**) = –69.5 (c = 1.15, CHCl$_3$). ESI-MS: 453 ([*M*+Na]$^+$).

(1'*R*)-[(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silyloxy]but-3-en-2-ol (138)

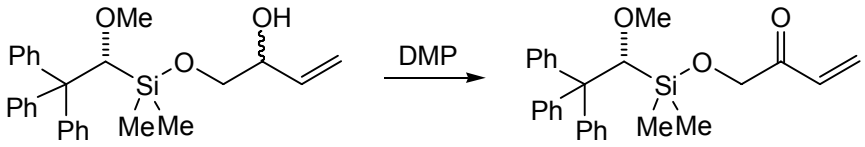


76b **138**

A soln. of **76b** (346.2 mg, 1.0 mmol) in CH_2Cl_2 (15.0 mL) was cooled to –78 °C, and Br_2 (0.054 mL, 1.05 mmol) was added drop wise. The cooling bath was removed, and the solvent evaporated under reduced pressure. The residual was dissolved in CH_2Cl_2 (20.0 mL), the mixture cooled to 0 °C, and NEt_3 (0.28 mL, 2.0 mmol), 3-Buten-1,2-diol (176.6 mg, 2 mmol), and DMAP (12.2 mg, 0.01 mmol) added. The mixture was stirred at 23 °C for 1 h, then quenched with H_2O (10 mL). The two layers were separated, the aq. phase extracted with Et_2O (2 x 20 mL), and the combined organic layers dried over $MgSO_4$. Evaporation of the organic fraction, and column chromatography (SiO_2; hexane/EtOAc 15:1) afforded **138** as a colorless oil (398.0 mg, 0.92 mmol, 92%). IR: 3450br.*m*, 2960*s*, 2922*s*, 1490*s*, 1455*s*, 1456*s*, 1250*s*, 1090*s*, 1080*s*, 830*s*. CI-MS: 257 (59); 92 (100). The NMR-data refer to the major isomer. ^{1}H-NMR: 7.31–7.14 (*m*, 15 arom. H); 5.78–5.66 (*m*, 1H, *H*C=CH$_2$); 5.32–5.12 (*m*, 2H, HC=C*H*$_2$); 4.42 (*s*, 1H, SiCH); 4.06–3.97 (*m*, 1H, (OH)C*H*); 3.50–3.42

(*m*, 2H, $SiOCH_2$); 3.32 (*s*, 3H, MeO); 2.26 (*s*, 1H, OH); –0.04, –0.38 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.9 (*s*, 3 arom. C); 136.6 (*d*, H*C*=CH_2); 130.1, 127.3, 126.0 (3*d*, 15 arom. C); 116.3 (*t*, HC=*C*H_2); 83.1 (*d*, SiCH); 72.7 (*d*, (OH)C); 66.5 (*t*, $SiOCH_2$); 61.2 (*q*, MeO); 60.7 (*s*, Ph_3C); –1.1, –2.1 (2*q*, Me_2Si).

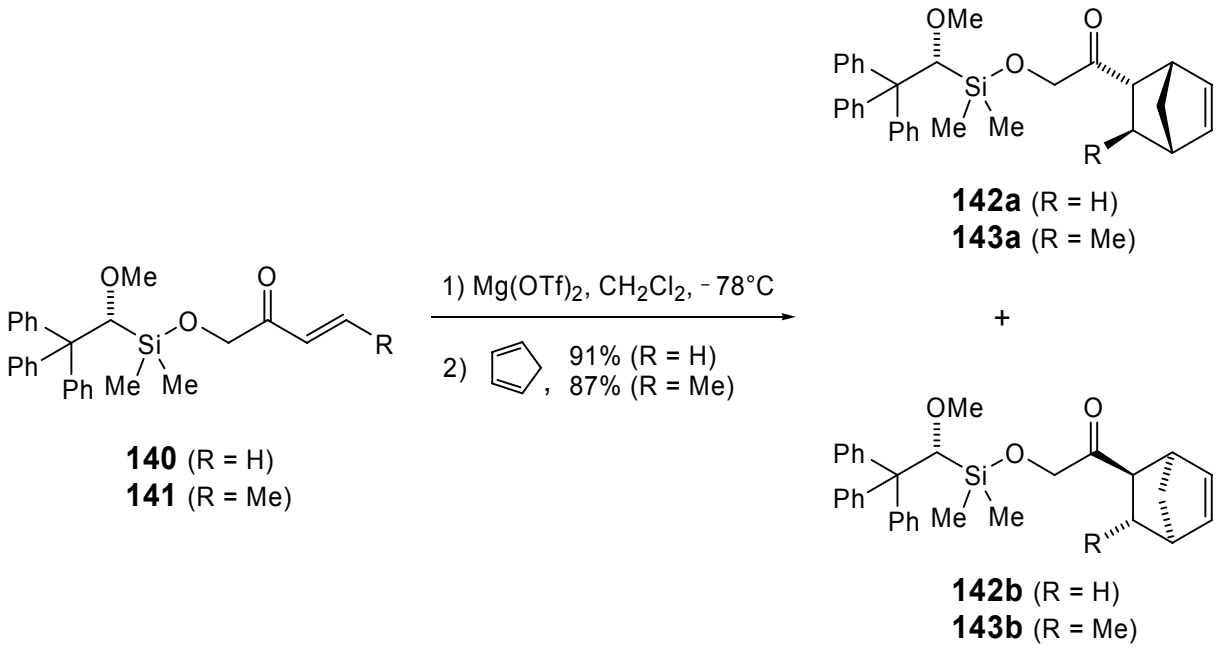
(1'*R*)-1-[(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)silyloxy]but-3-en-2-on (140)



138 **140**

DMP (2.2 mL of a 15% soln. in CH_2Cl_2, 1.02 mmol) was added to a soln. of **138** (293.7 mg, 0.68 mmol) in CH_2Cl_2 (7.0 mL) at 0 °C. After 10 min, the mixture was allowed to warm to 20 °C and stirred for 22 h. Then, MeOH (0.3 mL) was added. Evaporation of the combined organic fractions and column chromatography (SiO_2; hexane/EtOAc 20:1) afforded **140** (281.1 mg, 0.67 mmol, 97%) as a yellowish oil. IR: 2958*s*, 2924*s*, 1740*s*, 1700*s*, 1490*s*, 1445*s*, 1456*s*, 1250*s*, 1095*s*, 1080*s*, 830*s*. ^{1}H-NMR: 7.31–7.14 (*m*, 15 arom. H); 6.50 (*dd*, *J* = 10.3, 17.3, 1H, *H*C=CH_2); 6.27 (*dd*, *J* = 2.0, 17.3, 1H, HC=C*H*H); 5.74 (*dd*, *J* = 2.0, 10.3, 1H, HC=CH*H*); 4.46 (*s*, 1H, SiCH); 4.16 (*s*, $SiOCH_2$); 3.34 (*s*, 3H, MeO); –0.11, –0.32 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 198.3 (*s*, CO); 146.0 (*s*, 3 arom. C); 131.9 (*d*, H*C*=CH_2); 130.1, 127.4, 126.0 (3*d*, 15 arom. C); 128.6 (*t*, HC=*C*H_2); 83.7 (*d*, SiCH); 67.9 (*t*, $SiOCH_2$); 61.1 (*q*, MeO); 60.7 (*s*, Ph_3C); –1.3, –1.6 (2*q*, Me_2Si). $[\alpha]_D^{25}$(**140**) = –71.8 (c = 1.00, $CHCl_3$). ESI-MS: 453 ([*M*+Na]$^+$).

General procedure for the Diels-Alder reactions:



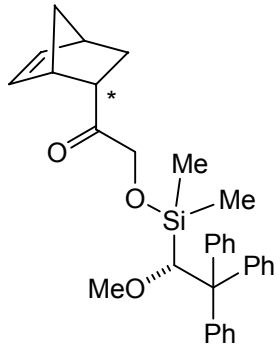
140 (R = H)
141 (R = Me)

142a (R = H)
143a (R = Me)

142b (R = H)
143b (R = Me)

A 1.0 M soln. of $Mg(OTf)_2$ in Et_2O (1.4 mL) was added to a solution of **140** or **141** (0.46 mmol) in CH_2Cl_2 (7.0 mL). The mixture was cooled to –78 °C, freshly distilled dicyclopentadiene (0.57 mL, 7.0 mmol) added, and then stirring prolonged for 20 min. After a filtration on a plough of SiO_2, and evaporation of the solvent under reduced pressure, the crude mixture was purified on column chromatography (SiO_2; hexane/EtOAc 25:1). Diastereoselectivities were established by integration of the signals correspondent to the Si*Me*$_2$ of the two diastereoisomers' absorptions in ^{1}H-NMR. Analytical data refer to the major isomer.

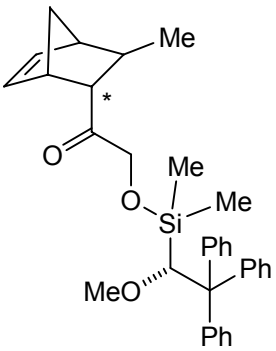
(1'*R*,1*S*,2*S*,4*S*)- and (1'*R*,1*R*,2*R*,4*R*)-1-(Bicyclo[2.2.1]hept-5-en-2-yl)-2-[(1-methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]ethanone (142a and 142b)



142a and **142b**

This compound was prepared from **140** (200.0 mg, 0.46 mmol), according to the general procedure. After purification, a mixture of **142a** and **142b** (180.7 mg, 0.36 mmol, 91%, *ds* > 99%) was obtained. IR: 3060*s*, 2970*s*, 2930*s*, 1720*s*, 1710*s*, 1490*s*, 1445*s*, 1436*s*, 1250*s*, 1092*s*, 1080*s*, 830*s*. ^{1}H-NMR: 7.31–7.14 (*m*, 15 arom. H); 6.17-6.14, 5.79–5.76 (2*m*, 2H, HC=CH); 4.46 (*s*, 1H, SiCH); 4.03, 3.96 (*AB*, *J* = 17.4, 2H, $SiOCH_2$); 3.35 (*s*, 3H, MeO); 3.16, 2.90 (2br.*s*. 2H, allylic); 3.10–3.04 (*m*, 1H, COCH); 1.77–1.22 (*m*, 4H, 2 CH_2); –0.09, –0.35 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 209.7 (*s*, CO); 146.0 (*s*, arom. C); 137.8, 131.3 (2*d*, HC=CH); 130.1, 127.4, 126.0 (3*d*, arom. C); 83.7 (*d*, SiCH); 68.6 (*t*, $SiOCH_2$); 61.1 (*q*, MeO); 60.7 (*s*, Ph_3C); 50.0 (*t*, CH_2); 47.3, 45.9, 42.6 (3*d*, 3 CH); 27.5 (*t,* CH_2); –1.3, –1.6 (2*q*, Me_2Si). ESI-MS: 519 ($[M+Na]^+$).

(1'*R*,1*S*,2*S*,3S,4*S*)- and (1'*R*,1*R*,2*R*,3R,4*R*)-1-(3-Methylbicyclo[2.2.1]hept-5-en-2-yl)-2-[(1-methoxy-2,2,2-triphenylethyl)dimethylsilyloxy]ethanone (143a and 143b)



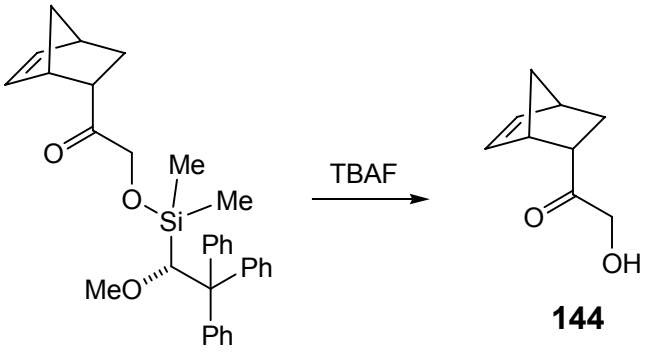
143a and **143b**

This compound was prepared from **141** (204.5 mg, 0.46 mmol), according to the general procedure. After purification, a mixture of **143a** and **143b** (204.4 mg, 0.40 mmol, 87%, *ds* > 99%) was obtained. IR: 3058*s*, 2964*s*, 2931*s*, 1717*s*, 1708*s*, 1490*s*, 1442*s*, 1439*s*, 1247*s*, 1090*s*, 1082*s*, 832*s*. ^{1}H-NMR: 7.68–7.46 (*m*, 15 arom. H); 6.60-6.53, 6.27–6.21 (2*m*, 2H, HC=CH); 4.79 (*s*, 1H, SiCH); 4.31, 4.24 (*AB*, *J* = 17.9, 2H, $SiOCH_2$); 3.67 (*s*, 3H, MeO); 3.16, 2.90 (2br.*s*. 2H, allylic); 3.10–3.04 (*m*, 1H, COCH); 1.41 (*d*, *J* = 6.5, 2H, CH_3CH); 1.28–1.12 (*m*, 4H, 2 CH_2); 0.20, –0.01 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 210.4 (*s*, CO); 147.1 (*s*, arom. C); 138.1, 132.0 (2*d*, HC=CH); 130.6, 127.7, 126.9 (3*d*, arom. C); 84.9 (*d*, SiCH); 68.9 (*t*, $SiOCH_2$); 61.5 (*q*, MeO); 60.8 (*s*, Ph_3C); 50.9 (*t*, CH_2);

47.6, 46.4, 42.9 (3*d*, 3 CH); 27.9 (*t,* CH_2); 26.4 (*q*, CH_3); –0.5, –1.1 (2*q*, Me_2Si). ESI-MS: 533 ([*M*+Na]$^+$).

5.3.2.2. Stereochemical assignments

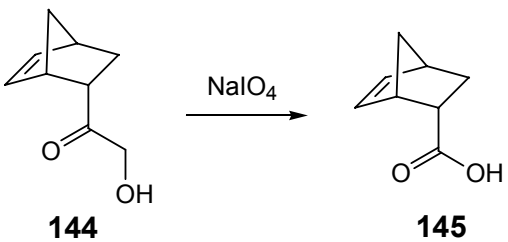
(1*S*,2*S*,4*S*)-1-(Bicyclo[2.2.1]hept-5-en-2-yl)-2-hydroxyethanone (144)



142a **144**

A soln. of TBAF in THF (1.0 M, 0.2 ml, 0.20 mmol) was added to a soln. of **142a** (50.0 mg, 0.10 mmol) in THF (2.0 mL) at 0 °C. After 15 min, a sat. aq. soln. of NH_4Cl (2 mL) was added. The two layers were separated and the aqueous phase was extracted with Et_2O (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure to afford the colorless oil **144** (14.9 mg, 0.097 mmol, 97%), which was used in the following step without further purification. $[\alpha]_D^{25}$(**144**) = –88.4 (c = 1.40, $CHCl_3$). IR: 3430*s*, 3060*s*, 1710*s*, 1570*s*, 1442*s*, 1459*s*, 1247*s*, 1090*s*, 1080*s*, 832*s*. ^{1}H-NMR: 6.16 (*dd*, 1H, *J* = 3.1, *J'* = 6.3, *H*C=CHCHCH); 5.81 (*dd*, 1H, *J* = 3.1, *J'* = 6.3, HC=C*H*CHCH); 4.38, 4.30 (*AB*, *J* = 16.5, OCH_2); 3.22 (br.*s*, OH); 3.40-2.65 (*m*, 3H, allylic, COCH); 1.44–1.29 (*m*, 2 CH_2).^{13}C-NMR: 210.4 (*s*, CO); 138.1, 132.0 (2*d*, HC=CH); 68.9 (*t*, OCH_2); 50.9 (*t*, CH_2); 47.6, 46.4, 42.9 (3*d*, 3 CH); 27.9 (*t,* CH_2). ESI-MS: 175 ([*M*+Na]$^+$).

(1*S*,2*S*,4*S*)-Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (145)



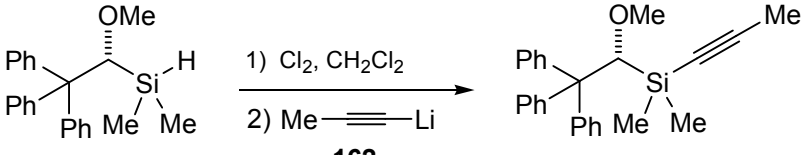
144 **145**

$NaIO_4$ (186.4 mg, 0.66 mmol) was added to a soln. of **144** (14.6 mg, 0.90 mmol) in a 1:1 mixture of CH_3CN/H_2O (5.0 mL), and it was stirred for 5 h at 23 °C. The mixture was then

extracted with Et_2O, an aq. soln. of NaOH (3.0 mL, 0.5 M) was added, and the two phases separated. The pH of the aq. phase was then corrected to 6-7 by addition of an aq. soln. of HCl (0.740 mL, 10%), Et_2O was added to the mixture and the two phases were again separated. The final organic layer was dried over $MgSO_4$ and filtered through a plough of silica gel to afford **145** (6.1 mg, 0.04 mmol, 67%) as a colorless solid. M.p. 33-34°C (from oil). $[\alpha]_D^{25}$ = –126.3 (c = 1.20, $CHCl_3$) [(1*S*,2*S*,4*S*)-**145**: $[\alpha]_D^{25}$ = –139.0 (c = 1.38, EtOH),[87] (1*R*,2*R*,4*R*)-**145**: $[\alpha]_D^{25}$ = +140.0 (c = 1.0 EtOH)[88]], confirming the configuration of **142a** as shown above. IR: 2986*s*, 1708*s*, 1570*s*, 1444*s*, 1460*s*, 1250*s*, 1090*s*, 1082*s*, 830*s*. ^{1}H NMR: 10.2 (br.*s,* COOH); 6.13 (*dd*, 1H, *H*C=CHCHCH, *J* = 2.9, J' = 5.7); 5.90 (*dd*, 1H, HC=C*H*CHCH, *J* = 2.9, *J'* = 5.5); 3.17 (br.*s*, COCH); 3.01-2.90 (*m*, 2H, allylic); 1.96–1.83 (*m*, 1H, *H*CHCHCH$_2$CHCO), 1.44–1.21 (*m*, 3H, HC*H*CHC*H*$_2$CHCO); ^{13}C-NMR: 181.0 (*s*, COOH) 137.8, 132.3 (2*d*, HC=CH); 49.7 (*t*, CH_2); 45.7, 43.3, 42.6 (3*d*, 3 CH); 29.1 (*t,* CH_2). CI-MS: 139 (100, $[M+H]^+$); 121 (10, $[M–H_2O+H]^+$).

5.4. Reactivity of substrates with MOTES directly linked to the carbon-framework

(1'*R*)-But-2-ynyl-(1-methoxy-2,2,2-triphenylethyl)dimethylsilane (157)

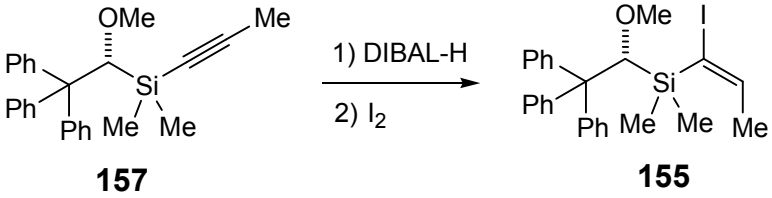


69b **162** **157**

A soln. of **69b** (3.46 g, 10.00 mmol) in CH_2Cl_2 (100.0 mL) was cooled to –25 °C, and Cl_2 was bubbled into the soln. for 1 min (till the complete consumption of **69b**, detectable on tlc). The cooling bath was removed, and the solvent evaporated under reduced pressure. The residual was then dissolved in THF (100.0 mL), the mixture cooled to –78 °C and a solution of 1-lithium-propyne, previously prepared from (*Z/E*)-1-bromo-1-propene (3.60 g, 30.00 mmol) and BuLi (1.6 M, 28.1 mL, 45.00 mmol) in THF (100.0 ml),[91] was added. The

mixture was stirred at 23 °C for 1 h, and quenched with H_2O (100 mL). The two layers were separated, the aq. phase extracted with Et_2O (2 x 100 mL), and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2, hexane/EtOAc 30:1) afforded **157** as a colorless oil (268.2 mg, 6.7 mmol, 67%). IR: 3046*s*, 2931*s*, 2854*s*, 2829*s*, 2440*s*, 1492*s*, 1444*s*, 1268*s*, 1106*s*, 1097*s*, 1071*s*, 941*s*. ^{1}H-NMR: 7.35–7.09 (*m*, 15 arom. H); 4.73 (*s*, 1H, SiCH); 3.61 (*s*, 3H, MeO); 2.01 (*s*, 3H, CCMe); 0.00, –0.18 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.8 (*s*, 3 arom. C); 130.0, 127.2, 125.8 (3*d*, 15 arom. C); 104.3, 84.3 (2*s*, *CC*Me); 82.6 (*d*, SiCH); 61.1 (*s*, Ph_3C); 60.9 (*q*, MeO); 4.8 (*q*, CC*Me*); 0.0, –1.7 (2*q*, Me_2Si). ESI-MS: 421 ([*M*+Na]$^+$).

(1'*R*)-(1-Iodo-propenyl)-(1-methoxy-2,2,2-triphenylethyl)dimethylsilane (155)

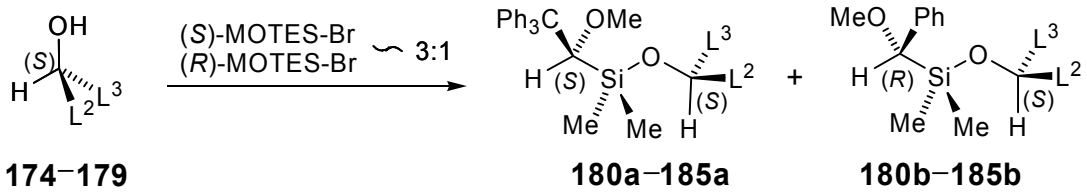


157 **155**

A soln. of **157** (400.46 g, 1.00 mmol) in Et_2O (10.0 mL) was cooled to 0 °C, and a soln. of DIBAL-H (20%, 0.460 mL, 1.10 mmol) was added. After 2 h resublimed I_2 (253.7 mg, 1.00 mmol) was added and stirred is prolongued at 23 °C for 3 h. The mixture was quenched with H_2O (10 mL). The two layers were separated, the aq. phase extracted with Et_2O (2 x 20 mL), and the combined organic layers were dried over $MgSO_4$. Evaporation of the organic fraction and column chromatography (SiO_2, hexane/EtOAc 40:1 to 10:1) afforded **155** as a colorless oil (30.3 mg, 0.06 mmol, 6%). ^{1}H-NMR: 7.35–7.09 (*m*, 16H, 15 arom. H + C*H*Me); 4.94 (*s*, 1H, CHSi); 3.43 (*s*, 3H, MeO); 1.69 (*d*, 3H, *J* = 8 Hz, CCH*Me*); 0.00, –0.61 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 146.4 (*d*, C*C*HMe); 145.9 (*s*, 3 arom. C); 129.9 (*d*, 3 arom. C); 127.4, 125.9 (*d*, 2 x 6 arom. C); 92.7 (*s*, CI); 82.2 (*d*, SiCH); 61.8 (*s*, Ph_3C); 60.9 (*q*, MeO); 8.7 (*q*, CC*Me*); 0.0, –1.7 (2*q*, Me_2Si). ESI-MS: 525 ([*M*+Na]$^+$).

5.5. MOTES as a chiral derivatizing agent

General procedure for the derivatization of alcohols:

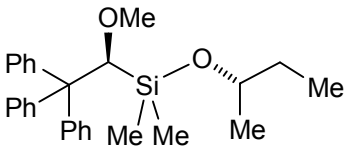


174–179 **180a–185a** **180b–185b**

A soln. of **69a** (259.6 mg, 0.75 mmol) and **69b** (86.5 mg, 0.25 mmol) in CH_2Cl_2 (15.0 mL) was cooled to –78 °C, then Br_2 (0.054 mL, 1.05 mmol) was added drop wise. The cooling bath was removed and the solvent evaporated under reduced pressure. The residual was dissolved in CH_2Cl_2 (20.0 mL), the mixture cooled to 0 °C, and NEt_3 (0.28 mL, 2.0 mmol), the desired alcohol **174–179** (2.0 mmol), and DMAP (12.2 mg, 0.01 mmol) were added. The mixture was stirred at 23 °C for 1 h, quenched with H_2O (10 mL), and the two layers were separated. The aq. phase was extracted with Et_2O (2 x 20 mL), the combined organic layers were dried over $MgSO_4$, and the solvent removed under reduced pressure.

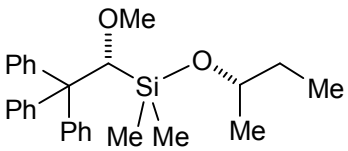
All the crude mixtures were analyzed by NMR spectroscopy, and then purified by flash chromatography (SiO_2; hexane/EtOAc 10:1). Signals of each isomer are assigned from analysis of ^{1}H-NMR spectra of the mixtures.

(1'*S*,2*S*)- and (1'*R*,2*S*)-2-Butoxy-(1-methoxy-2,2,2-triphenylethyl)dimethylsilane (180a and 180b)



180a

+



180b

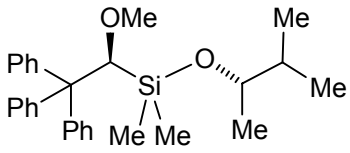
(*S*)-1-Butanol (**174**) (25.2 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **180a** and **180b** (142.2 mg, 0.33 mmol, 98%) was obtained as a colorless oil.

180a/**180b**: IR: 2980*s*, 2920*s*, 2880*s*, 2820*s*, 1490*s*, 1445*s*, 1250*s*, 1095*s*, 1080*s*. ESI-MS: 441 ([*M*+Na]$^+$).

180a: ^{1}H-NMR: 7.48–7.29 (*m*, 15 arom. H); 4.51 (*s*, 1H, SiCH); 3.89–3.68 (*m*, 1H, SiOCH); 3.49 (*s*, 3H, MeO); 1.62–1.51 (*m*, 2H, C*H*$_2$CH$_3$); 1.30–1.22 (*d*, *J* = 1.9, C*H*$_3$CH); 1.04–0.98 (*t*, *J* = 3.8, CH$_2$C*H*$_3$); 0.00, –0.32 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 146.5 (*s*, 3 arom. C); 130.3 (*d*, 3 arom. C); 127.7 (*d*, 6 arom. C); 126.1 (*d*, 6 arom. C); 84.2 (*d*, SiCH); 70.0 (*d*, SiOCH); 61.0 (*s*, Ph$_3$*C*); 60.9 (*q*, MeO); 32.4 (*t*, CH$_2$); 23.3 (*q*, CH*C*H$_3$); 10.2 (*q*, CH$_2$*C*H$_3$); 0.0, –1.0 (2*q*, Me$_2$Si).

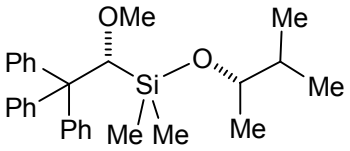
180b: ^{1}H-NMR: 7.48–7.29 (*m*, 15 arom. H); 4.53 (*s*, 1H, SiCH); 3.89–3.68 (*m*, 1H, SiOCH); 3.50 (*s*, 3H, MeO); 1.62–1.51 (*m*, 2H, C*H*$_2$CH$_3$); 1.31–1.23 (*d*, *J* = 1.9, C*H*$_3$CH); 1.06–0.99 (*t*, *J* = 3.8, CH$_2$C*H*$_3$); 0.00, –0.33 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 146.5 (*s*, 3 arom. C); 130.3 (*d*, 3 arom. C); 127.7 (*d*, 6 arom. C); 126.1 (*d*, 6 arom. C); 84.3 (*d*, SiCH); 70.0 (*d*, SiOCH); 61.0 (*s*, Ph$_3$*C*); 60.9 (*q*, MeO); 32.5 (*t*, CH$_2$); 23.5 (*q*, CH*C*H$_3$); 10.3 (*q*, CH$_2$*C*H$_3$); 0.1, –1.2 (2*q*, Me$_2$Si).

(1'*S*,2*S*)- and (1'*R*,2*S*)-(1,2-Dimethylpropoxy)-(1-methoxy-2,2,2-triphenylethyl) dimethylsilane (181a and 181b)



181a

+



181b

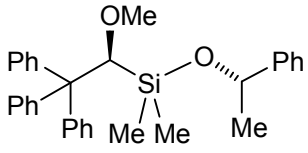
(*S*)-3-Methylbutan-2-ol (**175**) (29.9 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **181a** and **181b** (140.5 mg, 0.31 mmol, 98%) was obtained as a colorless oil.

181a/**181b**: IR: 2958*s*, 2920*s*, 2862*s*, 1490*s*, 1448*s*, 1250*s*, 1090*s*, 1085*s*. ESI-MS: 455 ([*M*+Na]$^+$).

181a: ^{1}H-NMR: 7.45–7.27 (*m*, 15 arom. H); 4.49 (*s*, 1H, SiCH); 3.74–3.63 (*m*, 1H, SiOCH); 3.47 (*s*, 3H, MeO); 1.79–1.67 (*m*, 1H, OCHC*H*); 1.20–1.12 (*d*, *J* = 4.19, C*H*$_3$CH); 1.04–0.98 (*m*, 6H, CH*Me*$_2$); 0.00, –0.33 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 146.4 (*s*, 3 arom. C); 130.4 (*d*, 3 arom. C); 127.9 (*d*, 6 arom. C); 126.3 (*d*, 6 arom. C); 84.3 (*d*, SiCH); 73.2 (*d*, SiOCH); 61.7 (*s*, Ph$_3$*C*); 61.1 (*q*, MeO); 35.5 (*t*, OCH*C*H); 20.3 (*q*, CH*C*H$_3$); 18.4 (*q*, CH*Me*$_2$); 0.0, –0.5 (2*q*, Me$_2$Si).

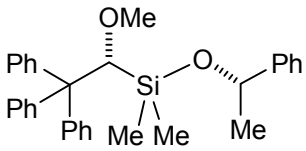
181b: ^{1}H-NMR: 7.45–7.27 (*m*, 15 arom. H); 4.51 (*s*, 1H, SiCH); 3.74–3.63 (*m*, 1H, SiOCH); 3.48 (*s*, 3H, MeO); 1.79–1.67 (*m*, 1H, OCHC*H*); 1.22–1.14 (*d*, *J* = 4.19, C*H*$_3$CH); 1.06–1.00 (*m*, 6H, CH*Me*$_2$); 0.00, –0.34 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 146.4 (*s*, 3 arom. C); 130.4 (*d*, 3 arom. C); 127.9 (*d*, 6 arom. C); 126.3 (*d*, 6 arom. C); 84.7 (*d*, SiCH); 73.5 (*d*, SiOCH); 61.7 (*s*, Ph$_3$*C*); 61.2 (*q*, MeO); 35.5 (*t*, OCH*C*H); 20.5 (*q*, CH*C*H$_3$); 18.6 (*q*, CH*Me*$_2$); 0.2, –0.7 (2*q*, Me$_2$Si).

(1'*S*,2*S*)- and (1'*R*,2*S*)-(1-Methoxy-2,2,2-triphenylethyl)dimethyl-(1-phenyl ethoxy)silane (182a and 182b)



182a

+



182b

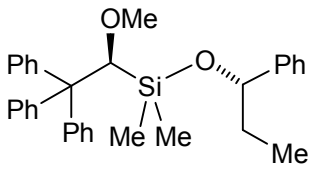
(*S*)-1-Phenylethanol (**176**) (41.5 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **182a** and **182b** (149.1 mg, 0.32 mmol, 98%) was obtained as a colorless oil.

182a/**182b**: IR: 2955*s*, 2920*s*, 2865*s*, 2850*s*, 1490*s*, 1448*s*, 1250*s*, 1105*s*, 1080*s*. ESI-MS: 489 ($[M+Na]^+$).

182a: ^{1}H-NMR: 7.58–7.31 (*m*, 20 arom. H); 4.78–4.62 (*m*, 1H, SiOCH); 4.49 (*s*, 1H, SiCH); 3.31 (*s*, 3H, MeO); 1.53–1.41 (*d*, J = 6.1, CHCH_3); –0.29, –0.42 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 147.5 (*s*, 3 arom. C); 145.6 (*s*, arom. C); 133.8, (*d*, 3 arom. C); 130.0 (*d*, 6 arom. C); 128.4, 127.9 (2*d*, 2 x 2 arom. C); 127.6 (*d*, 6 arom. C); 125.4 (*d*, arom. C); 83.4 (*d*, SiCH); 69.7 (*d*, SiOCH); 61.0 (*s*, Ph_3C); 62.3 (*q*, MeO); 25.7 (*q*, CHCH_3); 0.6, 0.2 (2*q*, Me_2Si).

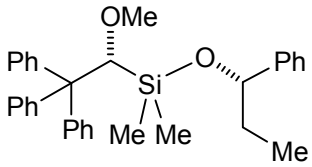
182b: ^{1}H-NMR: 7.51–7.23 (*m*, 20 arom. H); 4.70–4.60 (*m*, 1H, SiOCH); 4.55 (*s*, 1H, SiCH); 3.48 (*s*, 3H, MeO); 1.92–1.68 (*m*, CH_2CH$_3$); 1.53–1.41 (*d*, J = 6.1, CHCH_3); 0.00, –0.56 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 147.8 (*s*, 3 arom. C); 146.1 (*s*, arom. C); 134.0, (*d*, 3 arom. C); 130.3 (*d*, 6 arom. C); 128.7, 127.7 (2*d*, 2 x 2 arom. C); 127.3 (*d*, 6 arom. C); 126.0 (*d*, arom. C); 85.8 (*d*, SiCH); 69.5 (*d*, SiOCH); 60.7 (*s*, Ph_3C); 62.4 (*q*, MeO); 25.9 (*q*, CHCH_3); 1.0, –0.1 (2*q*, Me_2Si).

(1'*S*,2*S*)- and (1'*R*,2*S*)- (1-Methoxy-2,2,2-triphenylethyl)dimethyl-(1-phenylpropoxy) silane (183a and 183b)



183a

+



183b

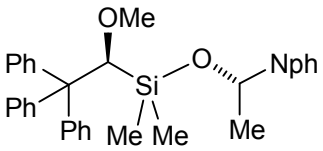
(*S*)-1-Phenylpropanol (**177**) (46.3 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **183a** and **183b** (144.0 mg, 0.30 mmol, 98%) was obtained as a colorless oil.

183a/**183b**: IR: 3050*s*, 2920*s*, 2860*s*, 2820*s*, 1490*s*, 1442*s*, 1250*s*, 1115*s*, 1095*s*, 1080*s*, 935*s*. ESI-MS: 503 ($[M+Na]^+$).

183a: ^{1}H-NMR: 7.51–7.23 (*m*, 20 arom. H); 4.70–4.60 (*m*, 1H, SiOCH); 4.52 (*s*, 1H, SiCH); 3.40 (*s*, 3H, MeO); 1.92–1.68 (*m*, CH_2); 1.04–0.93 (*t*, 3H, J = 7.2, CH_2CH_3); –0.20, –0.34 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 147.8 (*s*, 3 arom. C); 146.1 (*s*, arom. C); 134.0, (*d*, 3 arom. C); 130.3 (*d*, 6 arom. C); 128.7, 127.7 (2*d*, 2 x 2 arom. C); 127.3 (*d*, 6 arom. C); 126.0 (*d*, arom. C); 83.7 (*d*, SiCH); 69.5 (*d*, SiOCH); 60.7 (*s*, Ph_3C); 62.2 (*q*, MeO); 34.9 (*t*, CH_2); 11.4 (*q*, CH_2CH_3); 0.9, 0.4 (2*q*, Me_2Si).

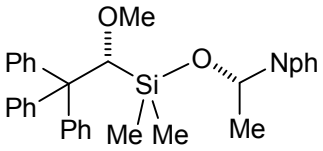
183b: ^{1}H-NMR: 7.51–7.23 (*m*, 20 arom. H); 4.70–4.60 (*m*, 1H, SiOCH); 4.58 (*s*, 1H, SiCH); 3.53 (*s*, 3H, MeO); 1.92–1.68 (*m*, CH_2); 1.04–0.93 (*t*, 3H, J = 7.2, CH_2CH_3); –0.00, –0.56 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 147.8 (*s*, 3 arom. C); 146.1 (*s*, arom. C); 134.0, (*d*, 3 arom. C); 130.3 (*d*, 6 arom. C); 128.7, 127.7 (2*d*, 2 x 2 arom. C); 127.3 (*d*, 6 arom. C); 126.0 (*d*, arom. C); 85.8 (*d*, SiCH); 69.5 (*d*, SiOCH); 60.7 (*s*, Ph_3C); 62.4 (*q*, MeO); 34.9 (*t*, CH_2); 11.6 (*q*, CH_2CH_3); 1.2, 0.0 (2*q*, Me_2Si).

(1'*S*,2*S*)- and (1'*R*,2*S*)-(1-Methoxy-2,2,2-triphenylethyl)dimethyl-(1-naphth-1-ylpropoxy)silane (184a and 184b)



184a

+



184b

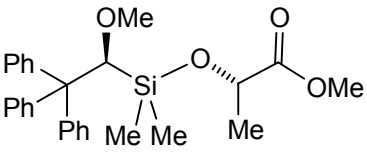
(*S*)-1-Naphth-1-ylethanol (**178**) (58.2 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **184a** and **184b** (165.3 mg, 0.32 mmol, 98%) was obtained as a colorless oil.

184a/**184b**: IR: 3090*s*, 3050*s*, 2920*s*, 2860*s*, 2820*s*, 1490*s*, 1442*s*, 1250*s*, 1115*s*, 1095*s*, 1080*s*, 935*s*. ESI-MS: 539 ([*M*+Na]$^+$).

184a: ^{1}H-NMR: 8.33–8.25, 8.12–8.06, 8.00–7.92, 7.89–7.78 (4*m*, 4 x arom. H); 7.73–7.62 (*m*, 2H, 2 x arom. H); 7.57–6.85 (*m*, 16 arom. H); 5.76–5.68 (*m*, 1H, SiOCH); 4.68 (*s*, 1H, SiCH); 3.51 (*s*, 3H, OMe); 1.78–1.73 (*d*, 3H, *J* = 6.5, CH*Me*); 0.00, –0.20 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.6 (*s*, 3 arom. C); 144.2 (*s*, arom. C); 134.2, 135.1 (2*s*, 2 arom. C); 129.9 (*d*, 3 arom. C); 129.6, 129.2, 129.8 (3*d*, 3 arom. C); 127.4 (*d*, 6 arom. C); 125.9 (*d*, 6 arom. C); 125.5, 124.6 (2*d*, 2 x 2 arom. C); 123.4, 123.5 (2*d*, 2 arom. C); 83.2 (*d*, SiCH); 68.8 (*d*, SiOCH); 61.1 (*s*, Ph_3C); 61.3 (*q*, MeO); 26.3 (*q*, $CHCH_3$); –0.2, –0.4 (2*q*, Me_2Si).

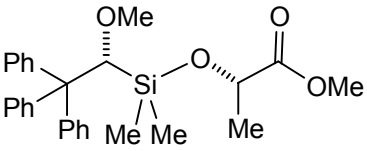
184b: ^{1}H-NMR: 8.33–8.25, 8.12–8.06, 8.00–7.92, 7.89–7.78 (4*m*, 4 x arom. H); 7.73–7.62 (*m*, 2H, 2 x arom. H); 7.57–6.85 (*m*, 16 arom. H); 5.76–5.68 (*m*, 1H, SiOCH); 4.72 (*s*, 1H, SiCH); 3.64 (*s*, 3H, OMe); 1.82–1.75 (*d*, 3H, *J* = 6.5, CH*Me*); 0.18, –0.38 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 145.9 (*s*, 3 arom. C); 144.2 (*s*, arom. C); 134.2, 135.1 (2*s*, 2 arom. C); 129.9 (*d*, 3 arom. C); 129.6, 129.2, 129.8 (3*d*, 3 arom. C); 127.4 (*d*, 6 arom. C); 125.9 (*d*, 6 arom. C); 125.5, 124.6 (2*d*, 2 x 2 arom. C); 123.4, 123.5 (2*d*, 2 arom. C); 83.3 (*d*, SiCH); 68.9 (*d*, SiOCH); 61.1 (*s*, Ph_3C); 61.5 (*q*, MeO); 26.4 (*q*, $CHCH_3$); 0.0, –0.7 (2*q*, Me_2Si).

(1'*S*,2*S*)- and (1'*R*,2*S*)-2-[(1-Methoxy-2,2,2-triphenylethyl)dimethylsilanyloxy] butyric acid methyl ester (185a and 185b)



185a

+



185b

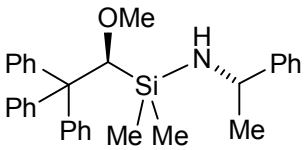
(*S*)-Methyl lactate (**179**) (40.1 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **185a** and **185b** (150.7 mg, 0.31 mmol, 98%) was obtained as a colorless oil.

185a/**185b**: IR: 2960br.*s*, 2860*s*, 2820*s*, 1770*s*, 1480*s*, 1442*s*, 1250*s*, 1115*s*, 1095*s*, 1080*s*, 935*s*. ESI-MS: 471 ([*M*+Na]$^+$).

185a: ^{1}H-NMR: 7.58–7.37 (*m*, 15 arom. H); 4.68 (*s*, 1H, SiCH); 4.41–4.32 (*s*, 1H, SiOCH); 3.91 (*s*, 3H, COO*Me*); 3.55 (*s*, 3H, CHO*Me*); 1.55–1.51 (*d*, 3H, *J* = 6.9, CH*Me*); 0.00, –0.12 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 146.3 (*s*, 3 arom. C); 130.5 (*d*, 6 arom. C); 127.7 (*d*, 6 arom. C); 126.2 (*d*, 3 arom. C); 83.7 (*d*, SiCH); 68.3 (*d*, SiOCH); 61.3 (*s*, Ph_3C); 61.0 (*q*, COO*Me*); 52.1 (*t*, CHCO*Me*); 21.4 (*q*, $CHCH_3$); –1.0, –1.1 (2*q*, Me_2Si).

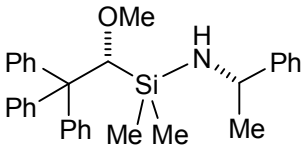
185b: ^{1}H-NMR: 7.58–7.37 (*m*, 15 arom. H); 4.72 (*s*, 1H, SiCH); 4.50–4.42 (*s*, 1H, SiOCH); 3.91 (*s*, 3H, COO*Me*); 3.58 (*s*, 3H, CHO*Me*); 1.60–1.56 (*d*, 3H, *J* = 6.9, CH*Me*); 0.16, –0.22 (2*s*, 6H, Me_2Si). ^{13}C-NMR: 146.3 (*s*, 3 arom. C); 130.5 (*d*, 6 arom. C); 127.7 (*d*, 6 arom. C); 126.2 (*d*, 3 arom. C); 84.2 (*d*, SiCH); 68.3 (*d*, SiOCH); 61.3 (*s*, Ph_3C); 61.0 (*q*, COO*Me*); 52.1 (*t*, CHCO*Me*); 21.6 (*q*, $CHCH_3$); 0.0, –1.8 (2*q*, Me_2Si).

(1'*S*,2*S*)- and (1'*R*,2*S*)-(1-Methoxy-2,2,2-triphenylethyl)dimethyl-(1-phenylethyl amino)silane (187a and 187b)



187a

+



187b

(*S*)-1-Phenylethylamine (**186**) (41.0 mg, 0.34 mmol) was derivatized according to general procedure. After chromatography a mixture of **187a** and **187b** (57.0 mg, 0.33 mmol, 36%) was obtained as a colorless oil.

187a/**187b**: IR: 3090br.*s*, 2920*s*, 2860*s*, 2820*s*, 1600*s*, 1490*s*, 1442*s*, 1250*s*, 1115*s*, 1095*s*, 1080*s*, 1000*s*.

187a: ^{1}H-NMR: 7.58–7.31 (*m*, 20 arom. H); 4.49 (*s*, 1H, SiCH); 4.00–3.89 (*m*, 1H, SiOCH); 3.31 (*s*, 3H, MeO); 1.53–1.41 (*d*, *J* = 5.9, CHC*H*$_3$); 1.38 (br.*s*, NH); 0.00, –0.09 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 147.5 (*s*, 3 arom. C); 145.6 (*s*, arom. C); 133.8, (*d*, 3 arom. C); 130.0 (*d*, 6 arom. C); 128.4, 127.9 (2*d*, 2 x 2 arom. C); 127.6 (*d*, 6 arom. C); 125.4 (*d*, arom. C); 83.4 (*d*, SiCH); 69.7 (*d*, SiOCH); 61.0 (*s*, Ph$_3$*C*); 62.3 (*q*, MeO); 25.4 (*q*, CH*C*H$_3$); 0.6, 0.2 (2*q*, Me$_2$Si).

187b: ^{1}H-NMR: 7.51–7.23 (*m*, 20 arom. H); 4.55 (*s*, 1H, SiCH); 4.00–3.89 (*m*, 1H, SiOCH); 3.48 (*s*, 3H, MeO); 1.92–1.68 (*m*, C*H*$_2$CH$_3$); 1.53–1.41 (*d*, *J* = 5.9, CHC*H*$_3$); 1.38 (br.*s*, NH); 0.10, –1.72 (2*s*, 6H, Me$_2$Si). ^{13}C-NMR: 147.8 (*s*, 3 arom. C); 146.1 (*s*, arom. C); 134.0, (*d*, 3 arom. C); 130.3 (*d*, 6 arom. C); 128.7, 127.7 (2*d*, 2 x 2 arom. C); 127.3 (*d*, 6 arom. C); 126.0 (*d*, arom. C); 85.8 (*d*, SiCH); 69.5 (*d*, SiOCH); 60.7 (*s*, Ph$_3$*C*); 62.4 (*q*, MeO); 25.5 (*q*, CH*C*H$_3$); 1.0, –0.1 (2*q*, Me$_2$Si).

5.6. X-ray crystal structure analysis

(±)-(1-Methoxy-2,2,2-triphenylethyl)(dimethyl)phenylsilane (70)

List of Tables

1. Experimental Details
2. Positional and Equivalent Isotropic Displacement Parameters for Non-H atoms
3. Bond Lengths
4. Bond Angles
5. Torsional Angles
6. General Atomic Displacement Parameter Expressions, U^{ij}'s
7. Positional and Displacement Parameters for Hydrogen Atoms

Figure Captions

1. *ORTEP*[1] representation of the molecule (50% probability ellipsoids; H-atoms given arbitrary displacement parameters for clarity)

Definition of Terms

Function minimized: $\Sigma w(F_o^2 - F_c^2)^2$

where $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$ and $P = (F_o^2 + 2F_c^2) / 3$

$F_o^2 = S(C - RB) / Lp$

and $\sigma^2(F_o^2) = S^2(C + R^2B) / Lp^2$

S = Scan rate

C = Total integrated peak count

R = Ratio of scan time to background counting time

B = Total background count

Lp = Lorentz-polarization factor

R-factors: $R_{int} = \Sigma|<F_o^2> - F_o^2| / \Sigma F_o^2$ summed only over reflections for which more than one symmetry equivalent was measured.

$R(F) = \Sigma||F_o| - |F_c|| / \Sigma|F_o|$ summed over all observed reflections.

$wR(F^2) = [\Sigma w(F_o^2 - F_c^2)^2 / \Sigma w(F_o^2)^2]^{1/2}$ summed over all reflections.

Standard deviation of an observation of unit weight (goodness of fit):

$[\Sigma w(F_o^2 - F_c^2)^2 / (N_o - N_v)]^{1/2}$

where N_o = number of observations; N_v = number of variables

Notes:

The structure of $C_{29}H_{30}OSi$ (mc.cph) has been solved and refined successfully with no unusual features. Since the space group is centrosymmetric, the compound in the crystal is racemic.

Experimental:

Crystal-Structure Determination – A crystal of $C_{29}H_{30}OSi$ was mounted on a glass fibre and used for a low-temperature X-ray structure determination. All measurements were made on a *Nonius KappaCCD* area-detector diffractometer[2] using graphite-monochromated Mo *K*α radiation (λ = 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. The unit cell constants and an orientation matrix for data collection were obtained from a least-squares refinement of the setting angles of 4382 reflections in the range 4° < 2θ < 50°. The mosaicity was 0.653(1)°. A total of 631 frames were collected using ϕ and ω scans with κ offsets, 20 seconds exposure time and a rotation angle of 1.0° per frame, and a crystal-detector distance of 35.0 mm.

Data reduction was performed with *HKL Denzo* and *Scalepack* [3]. The intensities were corrected for Lorentz and polarization effects, but not for absorption. The space group was uniquely determined by the systematic absences. Equivalent reflections were merged. The data collection and refinement parameters are given in *Table 1*. A view of the molecule is shown in the *Figure*.

The structure was solved by direct methods using *SIR92* [4], which revealed the positions of all non-hydrogen atoms. The non-hydrogen atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined by using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent atom ($1.5U_{eq}$ for the methyl groups). The refinement of the structure was carried out on F^2 by using full-matrix least-squares procedures, which minimised the function $\Sigma w(F_o^2 - F_c^2)^2$. The weighting scheme was based on counting statistics and included a factor to downweight the intense reflections. Plots of $\Sigma w(F_o^2 - F_c^2)^2$ versus F_c / F_c(max) and resolution showed no unusual trends. A correction for secondary extinction was applied. Five reflections, whose intensities were considered to be extreme outliers, were omitted from the final refinement.

Neutral atom scattering factors for non-hydrogen atoms were taken from Maslen, Fox and O'Keefe[5a], and the scattering factors for H-atoms were taken from Stewart, Davidson and Simpson[6]. Anomalous dispersion effects were included in F_c[7]; the values for f' and f'' were those of Creagh and McAuley[5b]. The values of the mass attenuation coefficients are those of Creagh and Hubbel[5c]. The *SHELXL97* program[8] was used for all calculations.

References:

(1) C.K. Johnson, *ORTEPII*, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.

(2) R. Hooft, *KappaCCD Collect Software*, Nonius BV, Delft, The Netherlands, 1999.

(3) Z. Otwinowski, W. Minor, in *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, Eds. C.W. Carter Jr., R.M. Sweet, Academic Press, New York, 1997, pp. 307-326.

(4) A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M.C. Burla, G. Polidori, M. Camalli, *SIR92*, *J. Appl. Crystallogr.* **1994**, *27*, 435.

(5) a) E.N. Maslen, A.G. Fox, M.A. O'Keefe, in 'International Tables for Crystallography', Ed. A.J.C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, pp. 477-486; b) D.C. Creagh, W.J. McAuley, *ibid*. Table 4.2.6.8, pp. 219-222; c) D.C. Creagh, J.H. Hubbell, *ibid*. Table 4.2.4.3, pp. 200-206.

(6) R.F. Stewart, E.R. Davidson, W.T. Simpson, *J. Chem. Phys.* **1965**, *42*, 3175-3187.

(7) J.A. Ibers, W.C. Hamilton, *Acta Crystallogr.* **1964**, *17*, 781-782.

(8) G.M. Sheldrick, *SHELXL97, Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, 1997.

Table 1. Crystallographic Data

Empirical formula	$C_{29}H_{30}OSi$
Formula weight [g mol^{-1}]	422.63
Crystal colour, habit	colourless, prism
Crystal dimensions [mm]	0.20 x 0.20 x 0.25
Temperature [K]	160(1)

Crystal system	monoclinic	
Space group	$P2_1/n$ (#14)	
Z	4	
Reflections for cell determination	4382	
2θ range for cell determination [°]	4 – 50	
Unit cell parameters	a [Å]	8.7240(1)
	b [Å]	11.6899(2)
	c [Å]	23.1937(5)
	α [°]	90
	β [°]	94.933(1)
	γ [°]	90
	V [Å^3]	2356.59(7)
$F(000)$	904	
D_x [g cm^{-3}]	1.191	
μ (Mo $K\alpha$) [mm^{-1}]	0.118	
Scan type	ϕ and ω	
2θ (max) [°]	50	
Total reflections measured	40642	
Symmetry independent reflections	4155	
R_{int}	0.052	
Reflections with $I > 2\sigma(I)$	3495	
Reflections used in refinement	4150	

Parameters refined	284
Final $R(F)$ [$I > 2\sigma(I)$ reflections]	0.0480
$wR(F^2)$ (all data)	0.1295
Weights:	$w = [\sigma^2(F_o^2) + (0.0474P)^2 + 1.9147P]^{-1}$ where $P = (F_o^2 + 2F_c^2) / 3$
Goodness of fit	1.107
Secondary extinction coefficient	0.013(2)
Final Δ_{max}/σ	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.62; -0.29
σ ($d_{(C-C)}$) [Å]	0.003 – 0.004

6. References

[1] I. Fleming, *Chem. Soc. Rev.* **1981**, *10*, 83.

[2] C. Eaborn, J. C. Jeffrey, *J. Chem. Soc.* **1954**, 4266.

[3] G. Stork, P. F. Hudrlik, *J. Am. Chem. Soc.* **1968**, *90*, 4462.

[4] D. J. Peterson, *J. Org. Chem.* **1968**, *33*, 780.

[5] J. A. Dale, H. S. Mosher, *J. Am. Chem. Soc.* **1972**, *95*, 512.

[6] E. Fischer, *Ber. Deutsch. Chem. Ges.* **1890**, *23*, 799.

[7] E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190.

[8] P. J. Kocienski, *Protecting Groups*, Georg Thieme Verlag Stuttgart, **1994**.

[9] K. K. Ogilvie, E. A. Thompson, M. A. Quilliam, J. B. Westmore, *Tetrahedron Lett.* **1974**, 2861.

[10] T. W. Green, *Protective groups in Organic Synthesis*, John Wiley & Sons, Inc., New York, **1981**.

[11] J. D. Morrison, J. W. Scott, in *Asymmetric Synthesis, Vol. 4* (Eds.: J. D. Morrison, J. W. Scott), Academic Press, Orlando, **1984**, p. 201.

[12] J. W. Scott, in *Asymmetric Synthesis, Vol. 4* (Eds.: J. D. Morrison, J. W. Scott), Academic Press, Orlando, **1984**, p. 1.

[13] L. D. Stegink, F. L., *Aspartame: Physiology and Biochemistry*, Marcel Dekker, Inc., New York, **1984**.

[14] S. Hanessian, *Total Synthesis of Natural Products: The "Chiron" Approach*, Pergamon, New York, **1983**.

[15] J. Seyden-penne, *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, John Wiley & Sons, Inc., New York, **1995**.

[16] R. A. Sheldon, *Chirotechnology*, M. Decker Ed., New York, **1993**.

[17] S. Masamune, W. Choy, J. S. Petersen, L. R. Sita, *Angew. Chem. Int. Ed.* **1985**, *24*, 1.

[18] I. Ojima, *Catalytic Asymmetric Catalysis*, VCH, Weinheim, **1993**.

[19] L. H. Sommer, *Stereochemistry, Mechanism and Silicon*, McGraw-Hill, New York, **1965**.

[20] L. H. Sommer, *Intra-Sci. Chem. Rep.* **1973**, *7*, 1.

[21] J. L. Fry, M. G. Adlington, *J. Am. Chem. Soc.* **1978**, *100*, 7641.

[22] R. J. P. Corriu, C. Guerin, J. J. E. Moreau, *Topics in Stereochemistry, Vol. 15*, Wiley, New York, **1984**.

[23] C. A. Maryanoff, B. E. Maryanoff, in *Asymmetric Synthesis, Vol. 4* (Eds.: J. D. Morrison, J. W. Scott), Academic Press, Orlando, **1984**, pp. 355.

[24] L. H. Sommer, C. L. Frye, G. A. Parker, K. W. Michael, *J. Am. Chem. Soc.* **1964**, *86*, 3271.

[25] L. H. Hathaway, L. A. Paquette, *J. Org. Chem.* **1983**, *48*, 3351.

[26] R. J. P. Corriu, J. Massé, *Tetrahedron Lett.* **1968**, 5197.

[27] R. J. P. Corriu, J. Massé, *Bull. Soc. Chim. Fr.* **1969**, 3491.

[28] R. J. P. Corriu, J. J. E. Moreau, *Nouv. J. Chim.* **1976**, *1*, 71.

[29] J. F. Klebe, *Acc. Chem. Res.* **1970**, *3*, 299.

[30] R. G. Daniels, L. A. Paquette, *Organometallics* **1982**, *1*, 1449.

[31] G. L. Larson, V. Cruz de Maldonado, L. M. Fuentes, L. E. Torres, *J. Org. Chem.* **1988**, *53*, 633.

[32] G. L. Larson, E. Torres, *J. Organomet. Chem.* **1985**, *293*, 19.

[33] B. F. Bonini, *Tetrahedron Lett.* **1991**, *32*, 6801.

[34] A. G. Brook, *Acc. Chem. Res.* **1974**, *7*, 77.

[35] S. Bienz, *Chimia* **1997**, *51*, 133.

[36] M. Oestreich, *Chem. Eur. J.* **2006**, *12*, 30.

[37] J. M. Brown, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **1994**, *116*, 866.

[38] A. J. Harrod, A. J. Chalk, in *Organic Synthesis via Metal Carbonyls, Vol. 2* (Eds.: I. Wender, P. Pino), Wiley, New York, **1997**, pp. 673.

[39] M. A. Brook, *Silicon in Organic, Organometallic, and Polymer Chemistry*, Wiley, New York, **2000**.

[40] D. Wang, T. H. Chan, *Tetrahedron Lett.* **1983**, *24*, 1573.

[41] M. E. Jung, K. T. Hogan, *Tetrahedron Lett.* **1988**, *29*, 6199.

[42] T. H. Chan, P. Pellon, *J. Am. Chem. Soc.* **1989**, *111*, 8737.

[43] K. Tamao, N. Ishida, M. Kumada, *J. Org. Chem.* **1983**, *48*, 2120.

[44] S. E. Denmark, B. D. Griedel, *J. Org. Chem.* **1994**, *54*, 317.

[45] B. F. Bonini, M. Comes-Franchini, M. Fochi, G. Mazzanti, A. Ricci, G. Varchi, *Synth. Lett.* **1998**, 1013.

[46] J. M. Seco, E. Quiñoá, R. J. Riguera, *Chem. Rev.* **2004**, *104*, 17.

[47] G. R. Weisman, in *Asymmetric Synthesis, Vol. 1* (Eds.: J. D. Morrison, J. W. Scott), Academic Press, New York, **1983**, p. 153.

[48] D. Parker, *Chem. Rev.* **1991**, *91*, 1441.

[49] R. Rotchild, *Enantiomer* **2000**, *5*, 457.

[50] M. G. Finn, *Chirality* **2002**, *14*, 534.

[51] P. L. Rinaldi, *Prog. Nucl. Magn. Spectrosc.* **1982**, *15*, 291.

[52] R. R. Fraser, in *Asymmetric synthesis, Vol. 1* (Eds.: J. D. Morrison, J. W. Scott), Academic Press, New York, **1983**, p. 173.

[53] E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley-Interscience, New York, **1994**.

[54] G. Uray, in *Methods in Organic Chemistry, Vol. 1* (Ed.: G. Houben-Weyl), Thieme, Stuttgart, **1996**, p. 253.

[55] J. M. Seco, E. Quinoà, R. Riguera, *Tetrahedron: Asymm.* **2001**, *12*, 2915.

[56] D. B. Weibel, T. R. Walker, F. C. Schroeder, J. Meinwald, *Org. Lett.* **2000**, *2*, 2381.

[57] F. C. Schroeder, B. D. Weibel, J. Meinwald, *Org. Lett.* **2004**, *6*, 3019.

[58] M. Trzoss, PhD thesis, Universität Zürich (2002).

[59] B. W. Wakefield, *Organomagnesium Methods in Organic Synthesis*, Academic Press, London, **1995**.

[60] J. Buynak, J. B. Strickland, G. W. Lamb, D. Khasnis, S. J. Modi, *J. Org. Chem.* **1991**, *56*, 7076.

[61] I. Fleming, R. S. Roberts, S. C. Smith, *Tetrahedron Lett.* **1996**, *37*, 9395.

[62] S. E. Bode, M. Wolberg, M. Müller, *Synthesis* **2006**, *4*, 557.

[63] A. R. Gallimore, J. B. Spencer, *Angew. Chem. Int. Ed.* **2006**, *45*, 4406.

[64] K. Soai, T. Hatanaka, T. Yamashita, *J. Chem. Soc., Chem. Commun.* **1992**, *124*, 9720.

[65] P. Knochel, W. Brieden, M. J. Rozema, C. Eisenberg, *Tetrahedron Lett.* **1993**, *34*, 5881.

[66] U. S. Racherla, H. C. Brown, *J. Org. Chem.* **1991**, *56*, 401.

[67] M. V. R. Reddy, A. J. Yucel, P. V. Ramachandran, *J. Org. Chem.* **2001**, *66*, 2512.

[68] G. E. Keck, J. A. Murry, *J. Org. Chem.* **1991**, *56*, 6606.

[69] D. J. Cram, A. Elhafez, *J. Am. Chem. Soc.* **1952**, *74*, 5828.

[70] D. J. Cram, D. R. Wilson, *J. Am. Chem. Soc.* **1963**, *85*, 1245.

[71] K. Kubota, J. L. Leighton, *Angew. Chem. Int. Ed.* **2003**, *42*, 946.

[72] X. Chen, E. R. Hortelano, S. V. J. Frye, *J. Am. Chem. Soc.* **1992**, *114*, 1778.

[73] K. Sa-ei, J. Montgomery, *Org. Lett.* **2006**, *8*, 4441.

[74] S. J. Stanway, E. J. Thomas, *Tetrahedron Lett.* **1995**, *36*, 3417.

[75] R. Chenevert, G. Fortier, R. B. Rhild, *Tetrahedron* **1992**, *48*, 6769.

[76] Y. Gao, B. Sharpless, *J. Org. Chem.* **1988**, *53*, 4081.

[77] G. Brulé, *Ann. Technol. Agric.* **1973**, *22*, 45.

[78] I. Yajima, T. Yanai, M. Nakamura, H. Sakakibara, K. Hayashi, *Agric. Biol. Chem.* **1984**, *48*, 849.

[79] R. G. Berger, G. R. Dettweiler, F. Drawert, *Deutsch. Lebensm.-Rdsch.* **1988**, *84*, 344.

[80] T. Bauerle, W. Schwab, *Phytochemistry* **1997**, *45*, 1153.

[81] D. L. Wright, J. W. Frankenfeld, United States Patent, Int. Pat. Nr. 3,836,672, 1974.

[82] J. W. Frankenfeld, M. Karel, T. P. Labuza, United States Patent, Int. Pat. Nr. 3,732,112, 1973.

[83] J. W. Frankenfeld, R. R. Mohan, R. L. Squibb, United States Patent, Int. Pat. Nr. 3,773,518, 1973.

[84] T. Bauerle, S. Engelhard, C. Bicchi, W. Schwab, *J. Nat. Prod.* **1999**, *62*, 35.

[85] T. Bauerle, P. Schreier, P. Brunerie, C. Bicchi, W. Schwab, *Phytochemistry* **1996**, *43*, 145.

[86] W. Carruthers, *Cycloaddition Reactions in Organic Synthesis, Vol. 8*, Pergamon Press, Oxford, **1990**.

[87] W. Choy, L. A. Reed, S. Masamune, *J. Org. Chem.* **2002**, *48*, 1137.

[88] C. Palomo, M. Oiarbide, J. M. García, A. González, A. Lecumberri, A. Linden, *J. Am. Chem. Soc.* **2002**, *124*, 10288.

[89] C. H. Krezdorn, G. Watsele, R. B. Kleene, *Eur. J. Biochem.* **1993**, *212*, 113.

[90] S. Bratovanov, S. Bienz, *Tetrahedron: Asymm.* **1997**, *8*, 1587.

[91] D. Toussaint, J. Suffert, *Org. Synth.* **1999**, *76*, 214.

[92] E.-I. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340.

[93] C. Piazza, P. Knochel, *Angew. Chem. Int. Ed.* **2002**, *41*, 3263.

[94] G. Righi, P. Bovicelli, A. Sperandio, *Tetrahedron Lett.* **1999**, *40*, 5889.

[95] F. A. Davis, R. E. Reddy, J. M. Szewczyk, G. V. Reddy, P. S. Portonovo, H. Zhang, D. Fanelli, R. T. Reddy, P. Zhou, P. J. Carroll, *J. Org. Chem.* **1997**, *62*, 2555.

CURRICULUM VITAE

Personal data

Name:	Maurizio Campagna
Date of birth:	13th April 1979
Nationality:	Italy

Education

1992–1997	Liceo scientifico "G. Seguenza", Messina (I)
1997–2002	M.Sc. degree, University of Bologna, Faculty of Industrial Chemistry, Bologna (I). Diploma thesis at the National Research Council (CNR): "Reazioni di addizione nucleofila ed amminazione elettrofila a composti α,β-insaturi" (Prof. Dr. A. Ricci and Dr. G. Varchi.
2003–2007	Ph.D. degree, University of Zurich, Institute of Organic Chemistry (Prof. Dr. Stefan Bienz). PhD thesis: "The MOTES-group as a multipurpose tool in organic synthesis"

Scientific publications during PhD studies:

M. Campagna, M. Trzoss, S. Bienz, **"**More than a Protective Group: Synthesis and Applications of a New Chiral Silane", *Org. Lett.* **2007**, 9, 3793–3796.

Scientific congresses during PhD studies:

2006	"1st European Chemistry Congress", Budapest (HU) (poster presentation)
2006	"Fall Meeting Swiss Chemical Society", Zürich (CH) (oral presentation)
2007	"Eight Tetrahedron Symposium", Berlin (D) (poster presentation)

ACKNOWLEDGEMENTS

Queste poche righe sono dedicate alle persone che hanno contribuito in maniera determinante alla realizzazione di questo lavoro. Le scriverò (almeno queste!) nella mia lingua, consapevole che tutti i destinatari — svizzeri e italiani — saranno in grado di comprenderla, anche se alcuni con qualche sforzo.

Sembra scontato dover citare il Prof. per primo. E invece a Stefan Bienz va la priorità assoluta di questi ringraziamenti non solo perché é stato il mio supervisor, professore preparato, e capace di insegnare chimica allo studente. A lui va il ringraziamento più sentito perché è riuscito a coniugare in modo davvero magistrale il concetto di rigore professionale con quello di comprensione umana: una medaglia con due facce che sono state per me, ora l'una ora l'altra a seconda delle situazioni, un continuo stimolo per migliorarmi e per proseguire con convinzione verso la fine dello studio. Per un giovane catapultato in una nuova avventura, all'estero, in un campo così imprevedibile come forse solo la chimica può essere, questo è un aiuto fondamentale e sarebbe impossibile non tenerne conto in questa sezione.

Accanto a lui, non posso non ringraziare tutti i compagni di laboratorio presenti e passati: Fabienne (discussioni infinite), Pascal (quante sere/notti passate insieme in lab!), Nadine (la voce giovane del gruppo), Michaël (e la "cou de boule" di Zidane), Silvan (l'uomo-birra), Denise (Miss Allegria, me la porterei dietro nel mio prossimo lavoro!) e poi il trio bulgaro con "Nonno" Boris, Nikolay e Lora (a quest'ultima sono grato per avermi introdotto alla silicon chemistry e al progetto che ho portato avanti), Dr. Laurent Bigler e Urs Stalder, tutti hanno una parte in questo lavoro. Un grazie speciale a

Manuel, Dok_2O, perché con lui ho diviso tanti momenti extra-lavorativi a me cari (a cominciare dalle innumerevoli sfide sui campi di basket…).

E poi tanta gente dell'università: tra questi Joëlle (una cara amica, svizzera ma nella mia testa sempre e solo italiana…e chissà perché...), Davide "Banderas" (lui sì un italiano, anzi lombardo (!), con un volume di voce del tutto tipico), Eliana (che non credo di poter considerare più solo una semplice collega di lavoro) e Francesca (con le nostre discussioni e i nostri appuntamenti a pranzo alle 13.59). Voglio anche ringraziare il professore Jay Siegel, non solo per essere il mio correlatore, ma anche per l'esempio di volontà e "voglia di fare" che ha trasmesso a me e a tanti altri nell'OCI.

Dall'Italia mi è arrivato anche il supporto della "kupola": Vito direttamente sul posto (quattro anni a Zurigo fatti di uscite, di scacchi, e di reciproca comprensione nei periodi bui), Adolfo (pochi mesi all'ETH, ma da lì in poi un costante collegamento), Alessandro (un insostituibile ormai nella mia vita), Antonio (una guida nei momenti di dubbi, un sorriso in quelli di scoraggiamento), Davidone (sentir lui per mezz'ora al telefono ricarica come nuovo) e Giuseppe (con la sua pazzia ed il suo affetto nei miei confronti).

E infine, per chiudere il cerchio lì dov'era iniziato (con le persone a priorità massima), c'è la mia famiglia: il papà e la mamma (ovvero quelli che avevano caldeggiato fin da subito questa esperienza e che mi hanno supportato fino al giorno dell'esame finale come solo i genitori fanno), Riccardo (un enorme aiuto pratico e tecnico, per tutto quello che ha implicato un trasferimento ed un'esperienza lavorativa all'estero), Ivana&Lio (per darmi sempre la sensazione di esser voluto bene anche "a distanza"), i tre nipotini (per tenere sempre vivo il mio buon umore) e Marisa (la mia seconda mamma e un orecchio sempre aperto per ogni problema). A tutti, un grazie di cuore.